CLINICAL AND AUDIO VESTIBULAR PROFILE OF MENIERE'S DISEASE IN A TERTIARY CARE CENTRE IN A DEVELOPING COUNTRY LIKE INDIA

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TO BE HELD IN FEBRUARY 2007

CERTIFICATE

This is to certify that the work presented in this dissertation, in partial fulfillment of the **Degree of MS Branch IV (ENT)** examination of **THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY** Chennai entitled **"CLINICAL AND AUDIOVESTIBULAR PROFILE OF MENIERE'S DISEASE IN A TERTIARY CARE CENTRE IN A DEVELOPING COUNTRY LIKE INDIA"** is the bonafide original work of **Dr. Paul Selvakumar.S,** post graduate student in **MS (ENT-Branch-IV)**. It was carried out and prepared under my overall guidance and supervision in the Department of Otorhinolaryngology and Head and Neck Surgery, Christian Medical College & Hospital, Vellore.

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INTRODUCTION

Meniere's disease is a clinical disorder first described by Prosper Meniere in 1861, characterized by fluctuating hearing loss, recurrent spontaneous episodic vertigo, tinnitus and aural fullness. Endolymphatic hydrops is the basic pathology in Meniere's disease in which dilatation of the endolymphatic spaces of membranous labyrinth due to excessive endolymphatic fluid. Both Meniere's disease and Meniere's syndrome are believed to result from increased pressure within the endolymphatic system. However, Meniere's disease is idiopathic, whereas Meniere's syndrome occur secondary to various processes interfering with normal production or resorption of endolymph e.g. trauma, autoimmune dysfunction, medications and syphilis etc. In atypical Meniere's disease patients will have some but not all the classical symptoms of Meniere's disease[1]. Cochlear Meniere's disease is recognized as a fluctuating sensorineural hearing loss and aural fullness in the absence of vestibular symptoms. Vestibular Meniere's disease[2] is characterized as episodic vertigo and disequilibrium associated with pressure in one or both ears.

Most of the symptom complex is subjective in nature, rendering critical analysis a problem. Difficulty in diagnosis of Meniere's disease due to waxing & waning nature, vague symptom complex, long period of remission and variable quality of data collection. Potential diagnosis for patients with vertigo is numerous. In spite of extensive evaluation, it is not uncommon for the

clinician to be unable to arrive at a precise diagnosis. At present, the inability to sample inner ear fluid pressures and analyze endolymphatic or perilymphatic chemical composition tent to make a precise diagnosis problematic at best. None of the currently available investigations gives definite evidence of endolymphatic hydrops. All the investigations gives only supportive evidence of endolymphatic hydrops. So detailed history and salient investigations are important to prevent misdiagnosis.

Once the diagnosis is established appropriate medication can be given & decision about need for destructive therapy in non responsive cases. Additionally it would also be useful to exclude the possibility of contra lateral disease.

Currently diagnosis of Meniere's disease is based on the diagnostic criteria of Meniere's disease designed by committee on Hearing equilibrium guidelines for 1995-American Academy of Otolaryngology-Head & Neck Surgery[3]. Accordingly Meniere's disease is classified into certain, definitive, possible & probable Meniere's disease.

A search of English literature showed no studies which described the clinical & audio vestibular profile in the Indian settings. Therefore this study was done to establish the frequency, clinical & audio vestibular profile of Meniere's disease in a specialized tertiary care hospital in South India.

AIMS AND OBJECTIVES

To find the frequency of the patients presenting with Meniere's disease using American Academy of Otolaryngology-Head & Neck Surgery diagnostic criteria in an Indian setting.

To describe the clinical and audio vestibular profile in these patients.

REVIEW OF LITERATURE

HISTORICAL ASPECT

"…for in science the successors stand upon the shoulders of their predecessors; where one man of supreme genius has invented a method, a thousand lesser men can apply it.

BERTRAND RUSSELL (1872-1970)

Meniere' disease has fascinated generations of physicians who have struggled to understand and explain the various features of this entity. Even Meniere himself could not have anticipated that the disease which bears his name would prove to be so enigmatic. Despite the world literature on Meniere's disease has become very vast; the amount of proven scientific knowledge is small. This resulted in lots of controversies regarding the nature of this disease, its pathophysiology, precise diagnosis and treatment.

In 1861, Dr. Prosper Meniere first described this disease which later named after him. This condition is characterized by recurrent episodes of vertigo, hearing loss, and tinnitus of sudden onset. These symptoms previously been called as 'apopletic cerebral congestion', a form of intracranial hemorrhage[4]. Experiments on birds done by Flourens[5] provides the first scientific clues that the semicircular canals in the inner ear were intimately involved in the regulation of balance. Meniere's novel concept that vertiginous

disorders were due to pathologic process in the semicircular canals was not accepted overnight, but realized only after another 70 years of scientific debate.

MENIERE'S DISEASE AFTER MENIERE

Meniere prophetically recognized that all forms of vertigo were not simply varieties of apopletic cerebral congestion. His papers urged his contemporaries for a better system of classification of vertiginous disorders. Instead, all forms of vertigo became grouped under vague headings of Meniere's syndrome and Meniere's syndrome complex[6]. The confusion within the medical community due to lack of understanding of vestibular physiology. In 1870 Friedrich Goltz concluded that semicircular canals were responsible for mediating equilibrium[7]. Knapp in 1871 suggest that Meniere's disease was the result of elevated intracochlear pressure, he termed as aural glaucoma[8]. Robert Barany in late 1800s advanced the understanding of vestibular physiology by introducing clinical exam for vestibular system, caloric testing, rotational testing and he explored the relationship between the semicircular canals and central nervous system[9]. For his achievements he was awarded Nobel Prize in 1915.

FUNCTIONAL ANATOMY OF VESTIBULAR SYSTEM

The vestibular system is the system of balance. It is also involved in the function of maintaining visual fixation during head movement and in maintaining posture and lower muscular control. An understanding of the anatomy and physiology of the normal vestibular system is the first step in being able to understand the symptoms, physical exam findings, and testing results during disease states.

Vestibular Apparatus (Figure 1)

The peripheral vestibular system is an integral part of the labyrinth that lies in the otic capsule in the petrous portion of the temporal bone[10]. Each vestibular apparatus is composed of a system of bony tubes and chambers located in the temporal bone called the bony labyrinth. Within this bony skeleton is a system of membranous tubes and chambers called the membranous labyrinth. The membranous labyrinth consists of the cochlea a part of the human auditory system and two types of vestibular organs: the semicircular canals and the otolith organs.The otolith organs are the utricle and saccule. These vestibular organs are the primary means by which we sense rotational and linear motion of the head, as well as the orientation of the head with respect to Earth's gravity. The entire membranous structure, which is filled with a viscous fluid called endolymph.

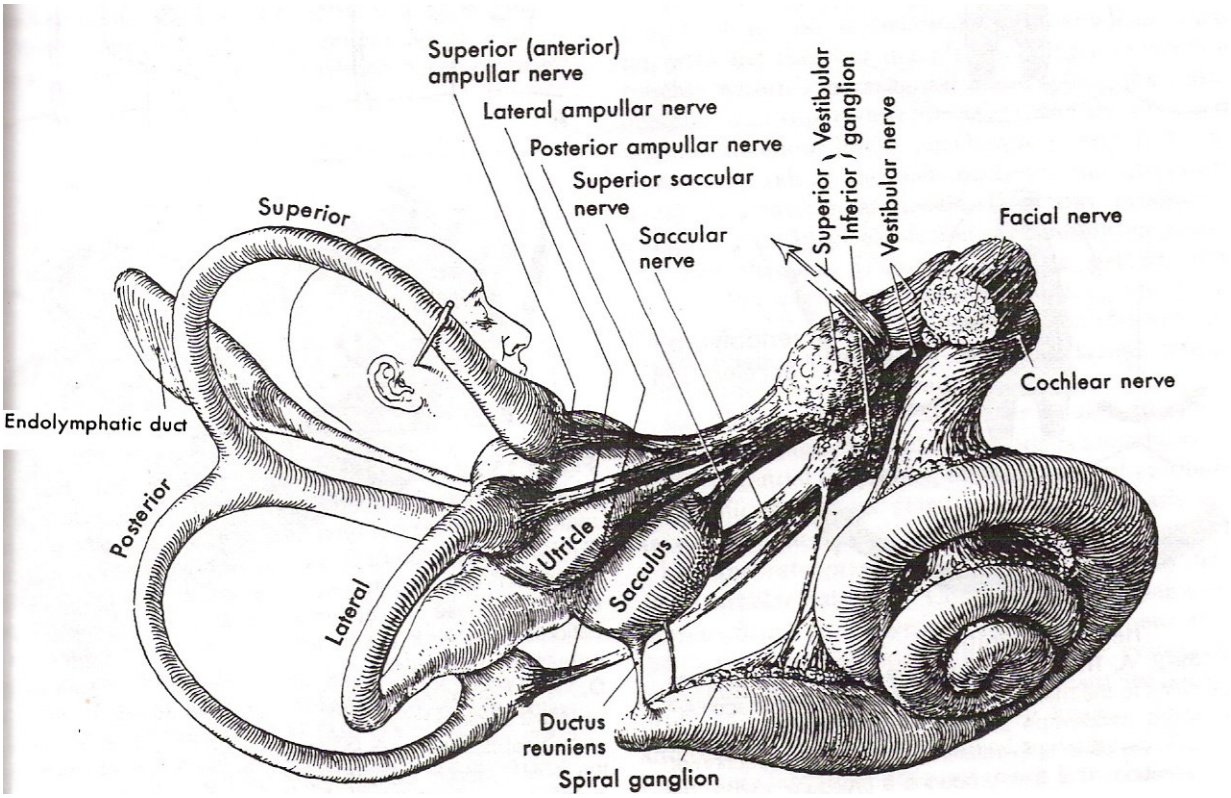


Figure 1: Peripheral vestibular system

Semicircular canals: The 3 semicircular canals are small ring like structures: lateral or horizontal, superior or anterior, and posterior or inferior. They are oriented at right angles to each other and are situated so that the superior and posterior canals are at 45° angles to the sagittal plane, and the horizontal canal is 30° to the axial plane. Each canal is maximally responsive to angular motion in the plane in which it is situated and is paired with a canal on the contralateral side so that stimuli that are excitatory to one are inhibitory to the other. The horizontal canal is paired with the contralateral horizontal canal; however, the superior canal is paired with the contralateral posterior canal and vice versa. Each canal forms two thirds of a circle with a diameter of about 6.5 mm and a luminal cross-sectional diameter of 0.4 mm[10]. One end of each canal is dilated to form the ampulla, which contains a saddle-shaped ridge termed the crista ampullaris, on which lies the sensory epithelium. The nonampulated ends of the superior and posterior canal form the crus commune or common crus. All canals merge into the utricle.

Membranous labyrinth (Figure 2)

Utricle: The utricle is larger than saccule and it situated posterosuperiorly to saccule in the elliptical recess of the medial wall of the vestibule. It is connected anteriorly via the utriculosaccular duct to the Endolymphatic duct. The 3 semicircular canals open into it by means of 5 openings; the posterior and the superior semicircular canals share one opening at the crus commune. The macula of the utricle lies mainly in the horizontal plane and is located in the utricular recess, which is the dilated anterior portion of the utricle.

Saccule: The saccule is an almost globular-shaped sac that lies in the spherical recess on the medial wall of the vestibule. It is connected anteriorly to the cochlear duct by the ductus reuniens and posteriorly to the endolymphatic duct via the utriculosaccular duct. The vestibular sensory epithelium is located on the maculae of the saccule and utricle and the cristae of the semicircular canals. The sensory cells are surrounded by supporting cells; therefore, they do not come into direct contact with the bony base of the cristae. The saccular macula is an elliptical thickened area of sensory epithelium that lies on the anterior vertical wall of the saccule.

Macula: Each macula is a small area of sensory epithelium. The ciliary bundles of the sensory cells project into the overlying statoconial membrane. The statoconial membrane is comprised of 3 layers.

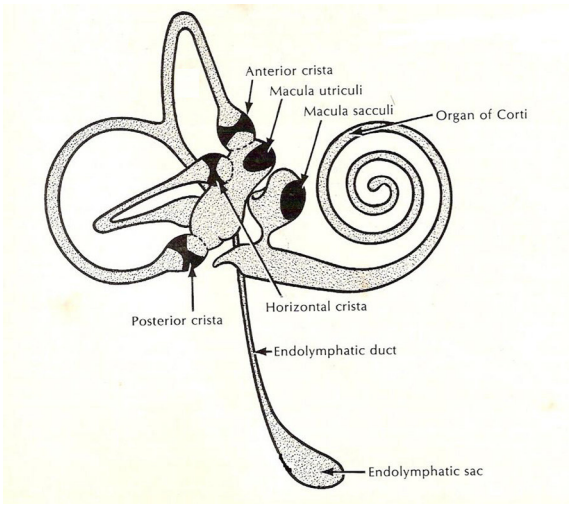


Figure 2: Membranous labyrinth

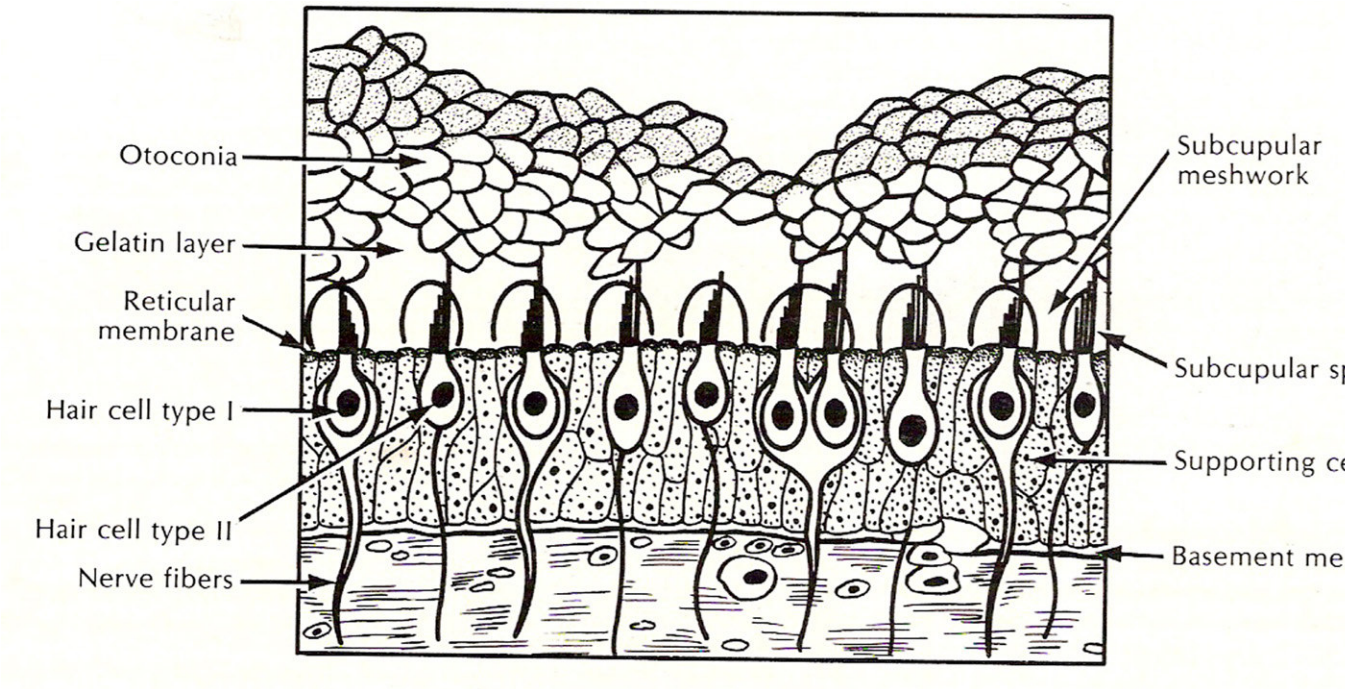
Otoconial membrane (Figure 3)

The otoconial first layer is comprised of calcareous particles (otoconia), which are inorganic crystalline deposits composed of calcium carbonate or calcite. They are distributed in a characteristic pattern and vary in size from 0.5-30 mcm, with most about 5-7 mcm. In the saccule, the largest otoconial are found close to the central strip (the striola) of the saccule, where as in the utricle, it is the smallest which lie near the striola, with the largest nearer the periphery of the macula. The specific gravity of the otolith membrane[10] is approximately 2.7.

The second layer is a gelatinous area of mucopolysaccharide gel.

The third layer consists of subcopula meshwork.

Figure 3: Otoconial membrane



The otoconia appear to have a slow turnover. They appear to be produced by the supporting cells of the sensory epithelium and to be resorbed by the dark cell region[11]. On a morphologic basis, each macula can be divided into 2 areas by a narrow curved zone that extends through its middle. This zone has been termed the striola.

Crista: The crista ampullaris consists of a crest of sensory epithelium supported on a mound of connective tissue, lying at right angles to the longitudinal axis of the canal. A bulbous, wedge-shaped, gelatinous mass called the cupula surmounts the crista. Cilia of the sensory cells project into the cupula. The cupula extends from the surface of the cristae to the roof and lateral walls of the membranous labyrinth, forming a fluid-tight partition.

Vestibular hair cells: The vestibular hair cells can be classified as type I or type II. Type I hair cells correspond to the inner hair cells of the organ of Corti and are flask shaped. Each cell is surrounded by a nerve chalice from one of the terminal branches of a thick or medium nerve fiber of the vestibular nerve. One calyx nerve ending can synapse with just one or two to four hair cells. Type II hair cells are cylinder shape corresponds to the outer hair cells of the organ of Corti and have multiple efferent and afferent bouton nerve synapses with a flat upper surface covered by a cuticle.

Sensory cells (Figure 4)

The sensory cells are neuroepithelial hair cells. Each bears 50-100 Stereocilia and a single thick and long kinocilium on the apical surface.

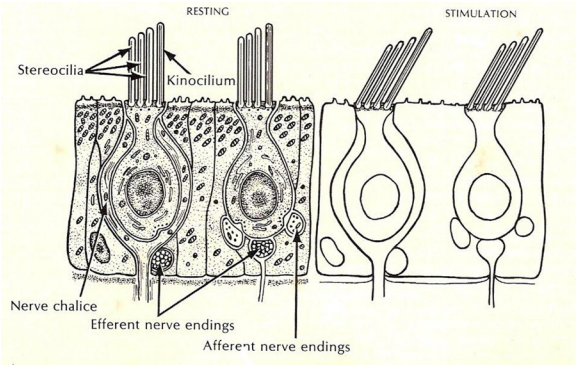


Figure 4: Vestibular sensory cells

Stereocilia: The Stereocilia, which are non motile and rigid, are not true cilia but consist of actin filaments in a paracrystalline array with other cytoskeletal proteins. The actin filaments in the Stereocilia extend into the hair cell and are anchored in a thickened region near the apical surface, termed the cuticular plate. The cuticular plate is a dense filamentous meshwork of randomly oriented actin filaments that fills up the area just under the apical surface of the cell. The Stereocilia vary in height but are graded with reference to the kinocilium in a staircase arrangement, the tallest being close to the kinocilium.

Kinocilium: The kinocilium projects from the cell cytoplasm through a segment of the cell lacking a cuticular plate. The kinocilium has a complete structure of a motile cilium with a basal body, which closely resembles the centriole and the 9+2 arrangement of microtubule doublets of true cilia[12].

However, the inner dynein arms are lacking, and a central pair of microtubules is not present in the distal portion of the kinocilium, suggesting that the vestibular kinocilia may be immotile or only weakly motile. Each hair cell is morphologically polarized with respect to location of the kinocilium.

The movement of the hair bundle toward the kinocilium causes an increase in the firing rate of the hair cell, while deflection away causes a decrease in the firing rate. In the lateral semicircular canals the kinocilium is located on the side nearest the utricle while in the superior and posterior semicircular canals the kinocilium is away from the utricle.

Supporting cells: Supporting cells that extend from the basement membrane to the apical surface surround hair cells. Their nuclei are usually found just above the basement membrane and below the hair cells. Hair cells form tight junctions and desmosomes with the supporting cells, thus separating the endolymphatic space in which endolymph bathes the Stereocilia above the cells, from the perilymphatic space below the apical surface.

Afferent vestibular pathways

The primary vestibular neurons are bipolar neurons whose cell bodies comprise the Scarpa ganglion in the internal auditory canal. These bipolar neurons lie in 2 linearly arranged cell masses extending in a rostral-caudal direction in the internal auditory canal. Each neuron consists of a superior and inferior cell group related to superior and inferior divisions of the vestibular nerve trunk.

The superior division supplies the cristae of the superior and lateral canals, the macula of the utricle, and the anterosuperior part of the macula of the saccule. The inferior division carries afferent from macula of the saccule and crista of the posterior canal through the foramen singulare, where it runs under round window, of Morgagni[13]. Medial to the vestibular ganglion, the nerve fibers of both divisions merge into a single trunk, which enters the brain stem.

CENTRAL VESTIBULAR CONNECTIONS

Vestibular nuclei: Most afferent fibers from the hair cells terminate in the vestibular nuclei, which lie on the floor of the fourth ventricle. They are bound medially by the pontine reticular formation, laterally by the restiform body, rostrally by the brachium conjunctivum, and ventrally by the nucleus and spinal tract of the trigeminal nerve. The central processes of the primary afferent vestibular neurons divide into an ascending and descending branch after entering the brain stem at the inner aspect of the restiform body. Some

primary vestibular neurons pass directly to the cerebellum, in particular the flocculonodular lobe and the vermis. No primary vestibular afferent neurons cross the midline.

In the vestibular nuclei, 4 major groups of cell bodies (the second-order vestibular neurons) may be identified—(1) superior vestibular nucleus (SVN) of Bechterew, (2) lateral vestibular nucleus (LVN) of Dieter, (3) medial vestibular nucleus (MVN) of Schwalbe, and (4) descending vestibular nucleus (DVN)[10]. Some nuclei receive only primary vestibular afferents, but most receive afferents from the cerebellum, reticular formation, spinal cord, and contralateral vestibular nuclei.

Macular afferents: The ascending ramus of utricular fibers terminates richly on cells throughout the ventral one third of the lateral vestibular nucleus; some of these pass on medially to terminate on large cells in the rostral one half of the medial vestibular nucleus. The descending ramus of utricular fibers terminates on cells (medium and large) in the rostral one third of the descending vestibular nucleus. Some of the ascending branches of the saccule innervate a small area in the lateral vestibular nucleus. The descending ramus of saccular nerves end on the same cells in the rostral one third of the descending nucleus as utricular and canal fibers.

Semicircular canals afferents: The ascending branches of the fibers from the superior and lateral canals terminate in the rostral part of the superior vestibular nucleus in a distribution of large and small fibers. After giving off

long collaterals in the nucleus, the ascending branches continue directly to the cerebellum. The incoming fibers from the posterior canal crista bifurcate more medially, and the ascending branches end in a more central and medial region of the superior vestibular nucleus and also probably continue to the cerebellum. The descending branches of fibers from the 3 cristae give collaterals mainly to the medial vestibular nucleus and, to a lesser extent, to the lateral and descending vestibular nuclei.

Projections from vestibular nuclei: The cells of the superior vestibular nucleus project in an ascending direction to the nuclei of the extra ocular muscles (III and IV). This projection reaches the ipsilateral eye nuclei by way of the medial longitudinal fasciculus. The lateral vestibular nucleus has been shown to be the sole source of fibers to the vestibulospinal tract. These fibers terminate near the anterior horn cells of all the spinal cord levels and mediate trunk and limb muscle reflexes. The descending vestibular nucleus appears to be the nucleus most clearly related to the cerebellum. The medial vestibular nucleus appears to be the least specialized of the complex. The efferent output projects in the median longitudinal bundle to both the oculomotor nuclei and the cervical cord. It is of important in coordinating eye, head and neck movements[10].

The vestibular area located in cerebral cortex temporal lobe near the auditory cortex. Functional MRI and PET studies implicate the insula as another possible cortical projection of the vestibular system.

LABYRINTHINE FLUIDS:

The labyrinth contains 2 distinctly separate fluids: the endolymph and the perilymph.

Endolymph: Among the extra cellular fluids of the body, endolymph has a unique ionic composition. The sodium (Na^+) content is low, and the potassium (K^+) content is high, which causes the endolymph to resemble intracellular rather than extra cellular fluid[10]. Endolymph is believed to be produced by the dark cells of the cristae and maculae, which are separated by a transitional zone from the neuroepithelium. The site of absorption of endolymph is presumably the endolymphatic sac, which is connected to the utricle and saccule by means of the endolymphatic, utricular, and saccular ducts. Experimental blockage of the endolymphatic duct produces endolymphatic hydrops, further suggesting that the endolymphatic sac is the primary site of absorption.

Perilymph: The ionic composition of perilymph is similar to that of extra cellular fluid and cerebrospinal fluid[10] (CSF). The site of perilymph production is controversial—it might be an ultra filtrate of blood, CSF, or both. Perilymph leaves the ear by draining through venules and through the middle ear mucosa.

Blood supply to the vestibular end organ: The main blood supply to the vestibular end organs is through the internal auditory (labyrinthine) artery, which usually arises from the anterior cerebellar artery, superior cerebellar artery, or basilar artery. Shortly after entering the inner ear, the labyrinthine artery divides into 2 branches known as the anterior vestibular artery and the common cochlear artery. The anterior vestibular artery provides the blood supply to most of the utricle, to the superior and horizontal ampullae, and to a small portion of the saccule. The common cochlear artery forms 2 divisions called the proper cochlear artery and the vestibulocochlear artery. The vestibulocochlear artery divides into a cochlear ramus and a vestibular ramus (also known as the posterior vestibular artery), which provide the blood supply to the posterior ampulla, the major part of the saccule, parts of the body of the utricle, and the horizontal and superior ampullae.

How do we sense angular accelerations

When the head begins to rotate, experiencing angular acceleration within the plane of semicircular canal, the inertia of the endolymph within the canal causes the fluid to remain stationary while the canal rotates with the head. This causes fluid to flow from the duct into the ampulla forcing the cupula to bow like a drumhead in the direction opposite to that of the rotation, thus, deflecting the cilia of the hair cells. As the head continues to rotate at a steady velocity, viscous forces between the canal and the endolymph cause the endolymph to "catch up" with the canal, eliminating the relative movement.

Elastic properties of the cupula then return it to a vertical position. With the cessation of spinning (angular deceleration), the moving fluid pushes against a suddenly still cupula and the cupula is deflected in the opposite direction[10]. It is in this manner that a semicircular canal senses rotational acceleration of the head about its particular axis of rotation.

Since the canals of the vestibular apparatus are orthogonal to one another, the labyrinth is able to detect rotation about any spatial axis because one or more semicircular canal is stimulated by any particular rotation. The same arrangement of semicircular canal is mirrored on both sides of the head. This implies that the canals on either side of the head will generally be operating in a push-pull rhythm; when one is excited, the other is inhibited and vice versa. It is important that both sides agree as to what the head is doing. If there is disagreement, i.e., if both sides push at once, then the person will feel debilitating vertigo and nausea.

The otolith organs are the primary means by which we sense linear acceleration of the head and the orientation of the head with respect to Earth's gravity. The otolith has greater specific gravity than the surrounding tissue and thus provides inertia[10]. When we initiate movement to one side in a linear manner, the mass of the otolith membrane and otolith produce a force on the hair cells cilia in the opposite direction according to Newton's Law:

Force = Mass x Acceleration

This force causes the cilia to bend. When experiencing constant velocity, the otolith reaches a state of equilibrium and we no longer perceive the motion.

The otolith organs also detect the orientation of the head with respect gravity. When the head is tilted, the direction of the force due to the acceleration of gravity changes with respect to the planes of the macula, causing the direction in which the hair cells are bent to change.

With the head erect, the macula of each utricle lies roughly in the horizontal plane, while that of each saccule lies roughly in the vertical plane. As a result, the utricle sense forces resulting from linear acceleration in the horizontal plane, i.e., front-to-back movement, left-to-right movement and combinations thereof. The saccule sense forces resulting from linear acceleration in the sagittal vertical plane, i.e. front-to-back movement, up-and-down movement and combinations movements.

Within each organ, the cilia brush complexes of hair cells are polarized and spatially arranged such that all possible directions of linear acceleration and head tilt are represented between the utricular and saccular otolith organs. That is, the brush piles of the hair cells are oriented such that any arbitrary tilt or movement excites a unique pattern of hair cells. This pattern appraises the nervous system of both the position of the head with respect to gravity and the direction of linear

acceleration of the head. The connections are also essential for the process of vestibular compensation following damage to one side of the ear. The visual contribution to the vestibular system gives origin to the so-called vestibular ocular reflex (VOR)[10]. The VOR is the vestibular response that is more amenable to clinical examination and manipulation. Another source of important input to the vestibular system is the lower limb input, which is essential for maintenance of posture.

In addition to the four major vestibular nuclei mentioned above, there are also small and disperse nuclei which probably receive different names in different species. Of the minor vestibular nuclei, the best known is the Y nucleus, which receives many connections from the saccule. Minor contributions to these classical works has been added in the last few decades, but our knowledge of how these connections contribute to the final control, equilibrium, and posture remains open for new research.

The vestibular ocular reflex (VOR): Visual contribution to the vestibular function contributes to the so-called vestibular ocular reflex. The VOR consists of the constant adjustments of the images in the retina of the eye by the nuclei of the brain stem which receives information from the eyes, the neck, trunk, cerebellum, and cerebral cortex. The semicircular canal-ocular reflex is the dominant reflex. The angular acceleration produces an exact mirror image of events which takes place simultaneously in opposite labyrinth. Each utricopetal stimulus in one labyrinth is matched by an equal, opposite,

utricofugal displacement in the paired canal of the other ear. Thus afferent information from right canal utricopetal movement exerts an excitatory influence on agonist muscles and an inhibitory influence on the antagonist muscles. This results in contraction of left rectus muscle and right medial rectus muscle with relaxation of the left medial rectus muscle, producing deviation of eyes to left side. Lack of coordination of the above inputs to the brain stem induces nystagmus[10].

The smooth pursuit system permits tracking of visual target with a smooth continuous movement of the eye thereby providing stable image protection to the fovea of the retina. The vestibule-cerebellum plays a dominant role in smooth pursuit[14].The saccadic system of eye movement control provides the fast component during the production of jerk nystagmus. The function of jerk nystagmus is to reposition a visual target of interest onto the fovea with a single rapid eye motion.The difference between the position of the target on the retina and the desired position on the fovea is known as retinal slip[15].

The optokinetic response is a combination of sooth pursuit and saccade mechanism. One system of oculomotor control is visual fixation. Another function of the vestibular system that can be measured clinically is body posture. Body posture depends on the information received from the antigravity muscles of the legs, as well as all the inputs mentioned above.

Meniere's disease

One of the common condition causing disturbance in the peripheral vestibular organ is Meniere's disease. Meniere's disease is defined as "a disease of membranous inner ear characterized by deafness, vertigo and usually tinnitus, which has as its pathologic correlate hydropic distension of the Endolymphatic system"[16].The additional symptom of aural fullness is often added to the current definition[17].

The term Meniere's syndrome implies that this group of symptoms occurs secondary to various processes that lead to interference with the normal resorption of endolymph, e.g. neurosyphilis, trauma and autoimmune disorders etc[18].Full blown attacks of Meniere's are probably caused by an increase in endolymphatic pressure that causes gross distention and rupture of Reissner's membrane which separating perilymph from endolymph(Figure 5) The potassium rich endolymph then bathes the vestibular nerve leading to a depolarization block and a transient loss of function, creating an acute vestibular imbalance, until the membrane is repaired and normal K -- Na relationships are restored[19].

Figure 5: Cochlea section showing distended Reissner's membrane

A physical distention leading to a mechanical disturbance of the utricle or saccule may also produce symptoms, for example, causing the otolith crises of Tumarkin, in which abrupt falling attacks of brief duration without loss of consciousness. In Lermoyez syndrome, the sudden sensorineural hearing loss which improves after the attack of vertigo. In atypical Meniere's disease patients will have some but not all the classical symptoms of Meniere's disease. Cochlear and vestibular Meniere's disease describe patient who have only auditory and vestibular symptoms respectively[2].

The prevalence & mode of presentation of Meniere' disease is widely variable. The incidence of Meniere's disease ranging from 36 to 157[20,21] per 100,000 people in developed countries. Extensive literature search does not revealed any prevalence rate in developing countries. The male: female ratio of definite cases of Meniere's disease was almost the same, and the age distribution peaked at the age group of 40--49 years for males, while the peak for females was at the age group of 30--39 years[22].The right and left ears are affected with equal frequency[23]. The incidence of bilateral involvement is variable. House et al[24] study showed the prevalence of bilateral Meniere's disease seen about 25%.

VERTIGO: The typical presenting history is episodic attack of typical rotatory vertigo (96.2%), with tinnitus (91.1%), ipsilateral hearing loss (87.7%)[25] and aural pressure in affected ear or on both sides 74.1%).he onset of vertigo may be preceded by an aura or with no warning[26] .Most of the episodes lasting 2-3

hours but 10% with less than 30 minutes and small with longer periods[27]. The number of vertigo attack about 3 to 4 per year in established Meniere's disease[28].The vertigo begins suddenly with severe spinning sensation and is accompanied by pallor, diaphoresis, nausea & vomiting.

According to AAO guidelines, the definitive spell of Meniere's attack is spontaneous rotational vertigo lasting at least 20 minutes (commonly several hours), is often prostrating, and is accompanied by nausea and commonly by vomiting or retching. Consciousness is not lost. During the definitive episode, horizontal rotatory nystagmus is always present. Meniere's disease, at least two definitive episodes of 20 minutes or longer must occur to permit the diagnosis of definite Meniere's disease[29].

SENSORINEURAL HEARING LOSS: Hearing loss is typically fluctuant and progressive, early in the disease low frequency hearing loss and flat losses in advanced disease. Some patient same sound perceived as a different pitch in the two ears called diplacusis binauralis dysharmonica. Greven AJ, Oosterveld W.J. established a minimal criterion for bilateral involvement is sensorineural hearing loss more than 15dB in the contralateral ear with concomitant tinnitus and recruitment[30].AAO criteria for hearing loss is average (arithmetic mean) of hearing thresholds at 0.25, 0.5, and 1 kHz is 15 dB or more higher that the average of 1, 2, and 3 kHz.

In unilateral cases, the average of threshold values at 0.5, 1, 2, and 3 kHz is 20dB or more poorer in the ear in question than on the opposite side.

In bilateral cases, the average of threshold values at 0.5, 1, 2, and 3 kHz is greater than 25 dB in the studied ear.

TINNITUS: Tinnitus may be first symptom of the disease and it may begin with the first attack. It is always present during spell. It may be continuous or intermittent and it is non pulsatile. Later tinnitus is constant and may result in being the primary complaint in the later stage of Meniere's disease. The pitch of the tinnitus tends to corresponds to the region of most severe hearing loss. Pitch was more commonly identified in low and medium frequencies[31]

AURAL FULLNESS: Aural fullness or aural pressure sensation most of the time limited to the ear, but some patient may constantly feel pressure elsewhere in the head & neck with attacks[32].

Committee on Hearing and Equilibrium of the American Academy of Otolaryngology-Head and Neck Surgery published recommended guidelines[33] for diagnosis and reporting the results of treatment of Meniere's disease as follows

Certain Meniere's disease: Definite Meniere's disease, plus histopathologic confirmation.

Definite Meniere's disease: Two or more definitive spontaneous episodes of vertigo 20 minutes or longer, audiometrically documented hearing loss on at least one occasion. Tinnitus or aural fullness in the treated ear. Other cases excluded.

Probable Meniere's disease: One definitive episode of vertigo, eudiometrically documented hearing loss on at least one occasion, Tinnitus or aural fullness in the treated ear. Other causes excluded

Possible Meniere's disease: Episodic vertigo of the Meniere's type without documented hearing loss, or sensorineural hearing loss, fluctuating or fixed, with disequilibrium but without definitive episodes. Other causes excluded.

AAO also devised a staging system based solely on hearing. Staging should only be applied retrospectively but should be used to characterize the patient's status just before treatment.

Stage Four-tone average at 0.5.1,2 and 3 kHz (For definite Meniere's disease only)

1) < or = 25dB

2) 26-40 dB

3) 41-70 dB

4) >70 dB

To assess the effects of episodic vertigo on daily activities, a six-point **functional level scale** is introduced which reflects how Meniere's disease affects a patient's activities.

1. My dizziness has no effect on my activities at all.
2. When I am dizzy I have to stop what I am doing for a while, but it soon passes and I can resume activities. I continue to work, drive, and engage in any activity I choose without restriction. I have not changed any plans or activities to accommodate my dizziness.
3. When I am dizzy, I have to stop what I am doing for a while, but it does pass and I can resume activities. I continue to work, drive, and engage in most activities I choose, but I have had to change some plans and make some allowance for my dizziness.
4. I am able to work, drive, travel, take care of a family, or engage in most essential activities, but I must exert a great deal of effort to do so. I must constantly make adjustments in my activities and budge my energies. I am barely making it.
5. I am unable to work, drive, or take care of a family. I am unable to do most of the active things that I used to. Even essential activities must be limited. I am disabled.
6. I have been disabled for 1 year or longer and/or I receive compensation (money) because of my dizziness or balance problem.

DIAGNOSTIC TESTS FOR MENIERE'S DISEASE

Evaluation of hearing loss by means of **pure tone audiometry** is very important in the diagnosis and staging of Meniere's disease. The loss is sensorineural. The nature of sensorineural hearing loss is non specific cochlear etiology. Early stage of the disease tends to be associated with low frequency sensorineural hearing loss. Commonly, the hearing loss is associated with loudness recruitment, distortion and reduced speech discrimination[34]. Most often demonstrate flat audiogram (42%) followed by peak pattern (32%), a downward sloping pattern(19%) and a rising pattern[35].Serial audiogram demonstrate fluctuation in the degree of sensorineural hearing loss. Recruitment can be elicited by alternate binaural loudness balance in unilateral disease or the loudness discomfort level in cases of bilateral disease. The middle ear pressure difference was significantly larger during periods of dizziness or recurrent dizziness than at the time of remission.[36]

Osmotic diuretics known to reduce cerebrospinal fluid and also dehydrate the endolymphatic hydrops. Based on this, Klockhoff and Lindblom developed **glycerol dehydration test** in 1966.[37]The dehydration of cochlea could reduce Endolymphatic volume and hydrops and hence improve peripheral auditory and vestibular function. Other diuretic agents used are furosamide, mannitol, ethanol, urea and isosorbide. Glycerol is preferred because it is simple, easily absorbed, can used as oral or intravenous route

and non toxic. In clinical practice positive glycerol test indicates reversibility and that treatment with diuretic drugs may be of value[38].Positive glycerol test interpreted by using either **Klockhoff criteria** (changes in PTA of >10dB in at least 3 consequent frequencies and/or changes in speech audiometry >12%) or **Snyder criteria**[39](changes in PTA of > 15 dB in at least 1 frequency and/or >10dB in any 2 frequencies for octave tests at 0.125-2 kHz and/or changes in speech audiometry of >12%. Akoika et al found 47% to have positive glycerol test.[40]The side effect of the test are head ache, nausea & diuresis[41].

Impedance audiometry: It is an objective test. Acoustic impedance measurement based on the principle that energy that is not absorbed by the ear is reflected. The test battery includes tympanometry and acoustic reflex testing.

Tympanometry based on the principle that when a sound strikes the tympanic membrane, some of the sound energy is absorbed while the rest is reflected. A stiffer membrane would reflect more sound energy than a compliant one. By changing the pressure of the external auditory canal, it is possible to find the stiffness of tympano ossicular system. The equipment has a probe which snuggly fits into the external ear canal, and it has three channels to deliver a tone of 220Hz, to pick up the reflected sound through a microphone and to bring about changes in air pressure in the ear canal. By charting the compliance of tympano-ossicular system against various pressure changes, different types of graphs called tympanogram. Type A is normal

tympanogram. Type B is flat graph which indicates middle ear fluid. Type C indicates negative middle ear pressure and Type D graph indicates ossicular discontinuity.

Acoustic reflex is based on the fact that a loud sound, 70-100dB above the threshold of hearing for a particular ear, causes bilateral contraction of stapedius muscle which can be detected by tympanometry. This is particularly used in detecting cochlear type of hearing loss.

Otoacoustic emissions (OAE) are an objective, non-invasive measure for evaluating outer hair cell activity. Otoacoustic emissions are generated by active cochlear processes, which are transmitted to the ear canal in a retrograde manner, through the cochlea to its base, through the ossicles, and then to the tympanic membrane. The tympanic membrane acts like a speaker diaphragm, allowing for the emission and detection of the cochlear “echoes.”

There are two types of otoacoustic emissions. They are spontaneous and evoked. As their name implies, spontaneous OAEs are emitted spontaneously, in the absence of external noise stimulation. They are found in 30% to 60% of normal ears. So it is not possible to identify whether the spontaneous OAE is from normal cochlear activity or hyperactive cochlear.

There are three types of evoked OAEs: Stimulus-frequency (SFOAEs), transiently evoked (TEOAEs), and distortion-product (DPOAE)[42]. SFOAEs are emitted in response to a constant low-level tone swept over a

specified frequency range. The recorded response lags in phase and is technically more difficult to measure and interpret than the other two types of evoked OAEs. TEOAEs are elicited with brief acoustic stimuli, consisting of either clicks or tone-bursts, and they are present in nearly all patients with a hearing threshold of less than 30 dB.

The third type of evoked OAE, distortion-product OAE (DPOAE), is elicited by the simultaneous application of two pure-tone frequencies to the ear. These primary tones are called f1 and f2, with f1 < f2. These cochlear signals originate from active movement of the cochlear outer hair cells These emissions are a result of nonlinear mechanical characteristics of the cochlea at a specific point and have a precise mathematical relation with the frequencies of the two eliciting primary tones f1 and f2. This frequency-selective property of distortion product otoacoustic emission suggests that they should be regarded as useful monitor of localized cochlear function at any predetermined frequency. Because endolymphatic hydrops causes cochlear malfunction, and both otoacoustic emissions and cochlear micro phonics measure specific cochlear activities. The DPOAE provide objective, frequency-specific information about the patient's cochlear function. The lack of consistent abnormal pattern and inability to test patient with anything more than mild hearing loss make this test less attractive. The absence of otoacoustic emission shown to be highly sensitive but non specific indicator of cochlear and middle ear dysfunction.[43]No consistent utility has been found for the use otoacoustic emission in testing for Endolymphatic hydrops.[44]

Electrocochleography: Electrocochleography (ECohG) has been used as an objective electrophysiological test that is useful in the clinical diagnosis of endolymphatic hydrops. Three electrical phenomena are interest in the ECohG evaluation. They include cochlear micro phonic, summating potential (SP) and action potential (AP). The negative summating potential (SP) is an essential component of ECohG, which is a reliable test to detect the presence of endolymphatic hydrops.[45]The absolute amplitude of the SP shows considerable variability across subjects.

A more consistent amplitude feature is the SP and action potential (AP) amplitude ratio (SP:AP). Electrocochleography has focused on the SP:AP ratio derived from alternating polarity click responses to confirm the diagnosis of Meniere's disease and to evaluate the results of treatment. The cochlear micro phonic is generated by hair cells in the cochlea and mirrors the input waveforms. Because acoustic compression and rarefaction waves create opposite polarity electrical events in the cochlea, alternating waves are averaged to eliminate the cochlear micro phonic.

There is usually a slight latency difference between the two APs evoked by condensation and rarefaction clicks. This difference has been reported to be the cause of widening of the AP, which is thought to be diagnostic for Meniere's disease. SP is a direct current (DC) end cochlear potential that follows the electrical envelope produced by a sound stimulus. When the basilar membrane is displaced toward the scala tympani, the negative

SP is enhanced. Electrode near the source with optimal electrical contact[46] showed that the transtympanic electrode consistently produces better signal-to-noise ratios and larger signal intensity compared with extra tympanic (ear canal) electrodes thus reducing averaging problems.

Extra tympanic electrodes[47]are placed at the most medial aspect of the ear canal but cannot significantly impede the movement of the tympanic membrane. All obtain a signal of lower potential and all require more averaging in order to separate the signal from background noise. Most investigators have used a value of 0.3 to 0.5 as the upper limit of normal for SP/AP ratio and found that approximately two thirds of Meniere's disease ears have abnormal ECohG results.[48] Transtympanic ECohG study performed by Orchik et al 75% of the patients showed SP: AP elevation[49]. Extra tympanic studies done by Pappas showed almost similar abnormal ECohG rates, ranging from 62%–68% in Meniere's disease populations[50].

Electronystagmography (ENG): is a study used to clinically evaluate patients with dizziness, vertigo, or balance dysfunction. ENG provides an objective assessment of the oculomotor and vestibular systems. The ENG has the advantage of determining qualitative characteristics and for quantitative analysis of the nystagmus. The standard ENG test battery consists of calibration or saccadic test, gaze nystagmus, optokinetic nystagmus, sinusoidal tracking test, positional test and caloric test.

Patients should discontinue all vestibulo sedative medications including alcohol atleast 48-72 hours prior to ENG test. Gaze and saccadic testing used dots placed on the wall and/or ceiling at specified places, optokinetic testing was conducted with a rotating drum with stripes of contrasting colors, and smooth pursuit testing was done with a swinging pendulum. The electro oculography objectively measures eye movements based on the principle of the cornea-retinal potential difference[51]; the cornea is electropositive relative to the retina. With a fixed recording site, voltage differences can be recorded for eye movements. Electrodes are placed around the patient's eyes to record the cornea-retinal potential differences. By placing electrodes on both a horizontal and vertical axis around the eyes, tracings are produced for eye movements on both axes. The videonystagmography using infrared wave technology provides the tracing made possible with darkness which eliminating the optic fixation.

The saccade test, also called the calibration test, evaluates the saccadic eye movement system. This system is responsible for rapid eye movements and refixation of the target on the fovea. Accuracy, latency, and velocity should all be taken into consideration when interpreting saccades. Gaze testing is conducted to evaluate for the presence of nystagmus in the absence of vestibular stimulation. Presence or absence of spontaneous nystagmus, exacerbation of nystagmus with addition of gaze tasks to stress the system and fixation suppression of spontaneous nystagmus is recorded. The smooth pursuit system is responsible for following targets within the visual

field. Tracking can be evaluated horizontally and vertically. The target may be a moving pendulum. The Caloric stimulation of the vestibular system offers an assessment of the lateral semicircular canal. This is a valuable tool because it allows for the objective measurement of function from each labyrinth individually. This test is considered non physiologic since isolating and stimulating one labyrinth at a time in nature is physiologically impossible testing done. The patient is placed in a reclining position with head at a 30° angle to make the lateral semicircular canal into vertical plane. Caloric stimulation can be accomplished with alternating binaural bithermal water irrigation in to the external auditory canal. To quantify the caloric tests two following formulae were used:

The vestibular paresis formula

$$CP= [(RC + RW) – (LC + LW)]/ RC + RW + LC + LW)] X 100$$

Normal range 0 to 20%

The directional preponderance formula

$$DP = (LC + RW) – (RC + LW))/ (RC + RW + LC + LW)] X 100.$$

Normal range 0 to 25%[51]

The most frequently ENG findings seen in Meniere's disease were unilateral caloric weakness (UW) in 49%, directional preponderance (DP) in 36%, and spontaneous and/or positional nystagmus (SN, PN) in 32%. ENG was normal in 25%. Bilateral caloric weakness (BW) occurred in 36% of patients with bilateral hearing loss[52].

MATERIALS AND METHODS

DESIGN: Prospective case series

All patients attending the audio vestibular clinic over a period of seven months from January 2006 to July 2006 were screened for the study. If they fulfilled the criteria for Meniere's disease as laid down by AAO 1995 and satisfied the inclusion & exclusion criteria, they were included in the study.

Inclusion criteria

Patients with true episodic vertigo or disequilibrium

Fluctuating hearing loss

Tinnitus/or aural fullness

Age between 5 to 75 years.

Exclusion criteria:

Chronic supurative otitis media of tubotympanic or atticoantral type

H/O Head injury

Autoimmune disorders

CNS abnormality on otoneurological examination and investigation

Typical BPPV presentation

Ototoxic drugs exposure

Mental retardation

Pregnant and lactating mothers.

METHODS

All consecutive patients aged between 5 years and 75 years presenting with the history of hearing loss, vertigo, tinnitus & or aural fullness who satisfying inclusion and exclusion criteria were included in this study. These patients were identified in the audio vestibular out patient clinic by using **vertigo evaluation form** (Annexure1) which includes detailed history, ENT examinations and detailed otoneurological examinations. The primary investigator will take them through the **preformatted structured questionnaire** (Annexure 2) which has incorporated in it all the variations of AAO criteria 1995. These patients will then undergo further investigations.

The blood investigations includes

Hemoglobin estimation
Blood sugar level
Fasting lipid profile
Serology test for Treponema pallidum

The audio vestibular investigations includes

Pure tone audiometry with glycerol if hearing loss present
Impedance audiometry
Electrocochleography (ECohG)
Distortion product Otoacoustic emission (DPOAE)
Electronystagmography **(**ENG)

The audio vestibular tests were done in the audio vestibular laboratory.

PURE TONE AUDIOMETRY: (Figure 6) This is done in the acoustically treated room. The pure tone audiogram done using properly calibrated GSI-61 clinical audiometer to establish the hearing loss.

Figure 6: Pure tone audiometry

Air conduction testing: A series of frequency specific pure tones were presented via ear phones asking the patient to respond each time he hears the sound stimulus. The audiologist find the auditory threshold which is defined as the softest intensity level at which a patient can hear the tone at least 50% of the time. The better ear is tested first. The head phone is placed over the opening of the external canal. The ears are tested individually and the threshold is obtained in dB at regular steps of 125, 250, 500, 1000, 2000, 3000, 4000, 6000 and 8000 kHz. The results are marked on the audiogram sheet.

Bone conduction testing: This involves placement of a bone conduction vibrator on mastoid process individually and finding thresholds at various

frequencies. Once the hearing loss is established, the patient was given the instruction about the glycerol pure tone audiogram. Patients were given 95% of oral glycerol at the dose 1.5 g /Kg with equal amount of juice after 4 hours of fasting. The pure tone audiogram was repeated at the interval of one & half hour and three hours after glycerol ingestion. The average hearing loss calculated with the sum of 500, 1000, 2000 & 3000 kHz. Glycerol test is consider to be positive if the hearing improved atleast 10 dB in 2 or three frequency (Figure 7 & 8) according to the Klockhoff and Lindblom criteria[39].

Figure 7: Pre glycerol pure tone audiogram

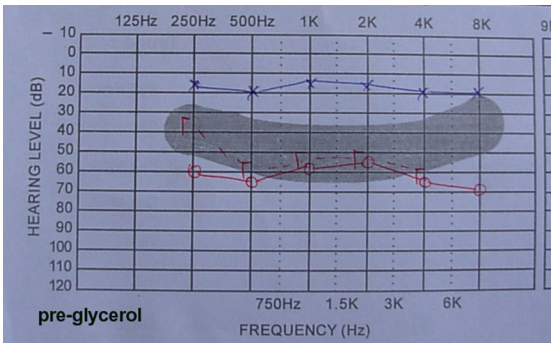
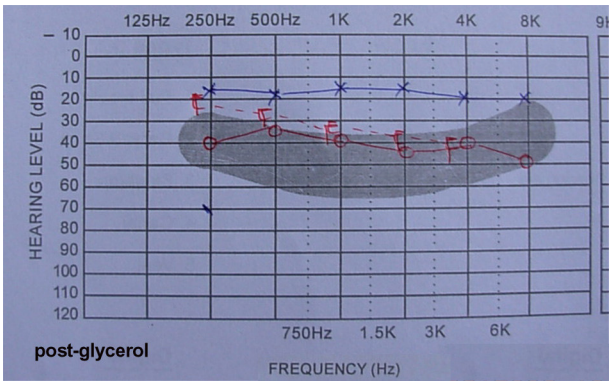


Figure 8: Post glycerol audiogram



IMPEDANCE AUDIOMETRY: The test battery includes tympanometry and acoustic reflex testing. The machine used in our lab was calibrated Siemens SD 30 Impedance audiometer. The head set involves an ear phone to be placed on the ear and a probe, to be inserted snugly into the canal of the other ear. The probe will deliver both a signal and changes air pressure towards the tympanic membrane and middle ear system, picking up the changes in the compliance and delivering those changes outwards for recording.

A pure tone stimulus (500- 4000 Hz) at 70-100dB above the threshold is delivered via ear probe as a reduction compliance of the middle ear system. The stimulus is increased or decreased until acoustic reflex threshold reported in dB is obtained. With ipsilateral acoustic reflex testing the pure tone is delivered via the probe and muscle contraction is recorded in the same ear, where as in contralateral reflex testing sound is delivered through head phone and muscle contraction is recorded in other ear by a probe placed in it[53].

ELECTROCOCHLEOGRAPHY (Figure 9)

Extra tympanic electrocochleography recordings were obtained using a commercial acoustic evoked potentials unit Opti-Amp 8000 Impedance Intelligent Hearing Systems and done in acoustically treated room. TIPtrode electrodes coupled to a tubal insert phone were placed into the external ear canal as deep as possible after cleaned with alcohol-impregnated cotton swabs. A horizontal recording montage was used with the primary electrode at

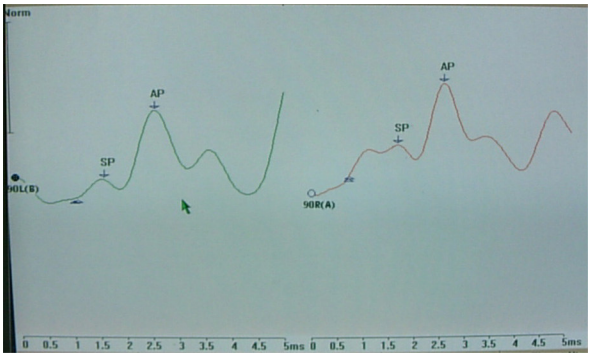
the ipsilateral ear canal and the secondary electrode at the contralateral earlobe. A low forehead-surface electrode served as the ground electrode. Two channel recordings were obtained using monaural stimuli consisting of alternating polarity clicks (90 dB normal hearing level) presented at a rate of 11.1 per second. Responses were averaged for 1,000 stimuli using a 10-ms time base. Each average was replicated at least two times. Evoked potential activity was band pass filtered from 3 to 1,500 Hz.

Figure 9: Electrocochleography

All recordings were plotted on an *x-y* plotter interfaced to the computer (Figure 10). Amplitudes were measured from the prestimulus baseline to the peak of the SP or AP. Normative value for SP AP ratio for extra tympanic ECohG in our lab previously been established as less than 0.5. The summating potential and action potential ratio of 0.50. or greater was used as

the diagnostic criterion for endolymphatic hydrops[54] and this was considered as abnormal value for the test.

Figure 10: Electrocochleography Tracing

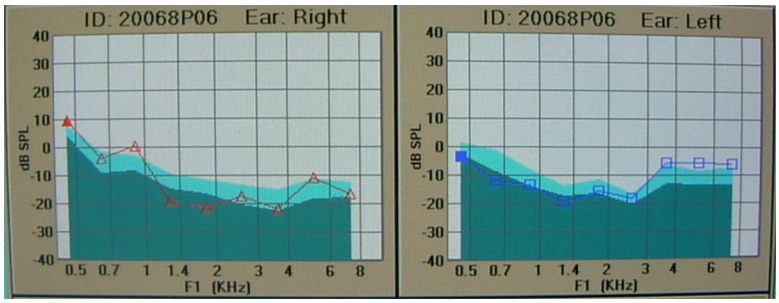


DISTORTION PRODUCT OTOACOUSTIC EMISSION (Figure 11)

DPOAE was recorded using the properly calibrated instrument OPTI-AMP 8000 Impedance Hearing Systems and the test was done in acoustically treated room. The probing system used was ER-100 ETYMOTIC OAE Probe.

Patient ear canal was cleaned and instruction given regarding avoidance of body movements including the swallowing movements. Probe is snuggly fit in the external auditory canal. The stimuli consist of 2 pure tones at 2 frequencies (f1 & f2 [f2> f1]) and 2 intensity levels.L1 & L2. An f1/f2 ratio yields the greatest DPOAE at 1.2 for low and high frequencies and at 1.3 for medium frequencies. Lowering the absolute intensity of the stimulus renders the DPOAE more sensitivity to abnormality. A setting of 65/55 dB is frequently used. The response is recorded at the emitted frequency of 2 f1-f2. DPOAE is consider present when the DPOAE have 3 to 6dB amplitude above the noise floor for each frequency (Figure 12). Presence of wave above the noise floor indicates normal test and the wave below the noise floor indicates absent DPOAE response.

Figure 12: Distortion product otoacoustic emission graph



ELECTRONYSTAGMOGRAPHY (Figure 13)

Patients should be advised to limit food intake prior to examination valuation, to avoid frequent blinking, to stop certain medications such as sedatives, tranquilizers and antivertigo medications 48 hours before the tests.

Figure 13: Electronystagmography

Single channel ENG machine, records conjugate eye movements and can give useful information in a dizzy patient. The test begins with the patient sitting comfortably in an adjustable chair in a room with no electrical disturbance or interference. The patient's skin is cleaned well with spirit. Electrode jelly is applied on the electrodes to minimize electrode-skin resistance. Electrodes are fitted on both the outer canthi of the eyes, with the neutral electrode on the forehead, using lead free adhesive tapes.

The ENG procedure consists of the following steps:

Biocalibration is done by using a calibration bar. The patient is asked to look at two LED lights that flash alternatively, kept at a distance of 40 degrees in front of the patient (20 deg to right, 20 deg to left). This information is used to calculate amplitude and slow phase velocity of nystagmus. It can also give information about proper fixing of electrodes and correctness of polarity of fixed electrodes.

Pendular test: The patient is asked to look at the moving pendulum which moves through an arc which subtends an angle of 40 degrees in front of the patient and the eye movement is recorded on the ENG. This pattern of movement can be used to assess the smooth pursuit system.

Spontaneous nystagmus: The patient is seated upright and eyes are centered. Recording is taken with eyes open for one minute and closed for one minute.(only the latter 30 secs of each minute are taken for calculation).During this test coordination in both eyes are noted and nystagmus >19 in 30 sec is considered abnormal

Gaze-evoked nystagmus is defined as nystagmus which appears on gaze deviation in one or more directions and is not present in mid-position. The patient is asked to look at a point 30 degrees to the right and to the left, up and down. Recording of eye movements is done in each gaze position for one minute. It is pathological if the amplitude is >4 degrees, or there are more than 19 nystagmus in 30 secs.

Caloric testing: A soft rubber catheter is applied deep in the meatus of the ear under vision. The patient lies supine, with head end elevated by 30

degrees from the horizontal position. Opposite ears are irrigated alternatively with 20 ml of water at 44 degrees Celsius and 30 degrees Celsius for 30 sec in each ear in the following order. Right 44 left 44, right 30 & left 30 degrees[52]. Recording is done for 2 minutes. The patient is asked to close the eyes and to keep alert during the procedure doing simple arithmetic (e.g. subtracting 7 from 700). After 90 secs of recording, the patient is asked to open the eyes and for just a 30 second period, asked to look at a point in front. The recording is done again to assess suppression by optic fixation. An interval of 8 minutes is given between each successive irrigation.

Recording of the caloric test is done by videonystagmographic recording using the computerized Hortmann machine which makes use of the Jongkee's formula based on slow component velocities (in degrees per second) and duration of the nystagmus during the cumulative phase of the nystagmus

The Jongkees' formula for vestibular paresis formula

$$CP= [(RC + RW) - (LC + LW)]/ RC + RW + LC + LW)] \times 100$$

Normal range 0 to 20%

The Jongkees' formula for directional preponderance formula

$$DP = (LC + RW) - (RC + LW))/(RC + RW + LC + LW)] \times 100.$$

Normal range 0 to 25%[52]

Statistical analysis

The descriptive biostatistical analysis was done using SPSS (Statistical package for social Science) version 11.0.The statistical method used was frequency and cross tabulation for the variables.

RESULTS

Frequency of Meniere's disease

The number of new patients who attended the Audio vestibular clinic (AVC) of Christian Medical College Hospital between January 2006 to July 2006 were 447. Among these 70 patients provided a history that suggested they may have Meniere's disease, a frequency of 15.6% (70 / 447).

Types of Meniere's disease according to AAO Criteria

The totals of 70 patients were sub classified according to the AAO 1995 criteria (Table 1 and figure 14). The largest group (76%) had definite Meniere's disease.

Definite Meniere's disease were 53 (n=76%)

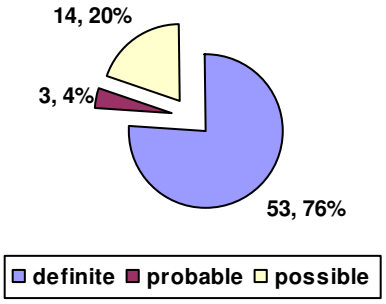
Probable Meniere's disease were 3 (n=4%)

Possible Meniere's disease were 14 (n=20%)

TABLE 1: TYPES OF MENIERE'S DISEASE

Diagnosis	No. of patients	Percent
Definite Meniere's	53	76%
Probable Meniere's	3	4%
Possible Meniere's	14	20%
Total	70	100%

Figure 14: Types of Meniere's disease (AAO Criteria)



Clinical Profile of patients with Meniere's disease

Age distribution

In this study the patients were between the age of 19 and 70 years; 16 (23%) were between 26 and 40 years and 33 (47%) were between the age of 41 and 55 years. The mean age for males was 45 years and females was 39 years (Table 2 and figure 15)

Table 2: AGE DISTRIBUTION

Age group	No. of patients	Percent
10-25	7	10%
26-40	16	23%
41-55	33	47%
56-70	13	19%
>70	1	1%
Total	70	100%

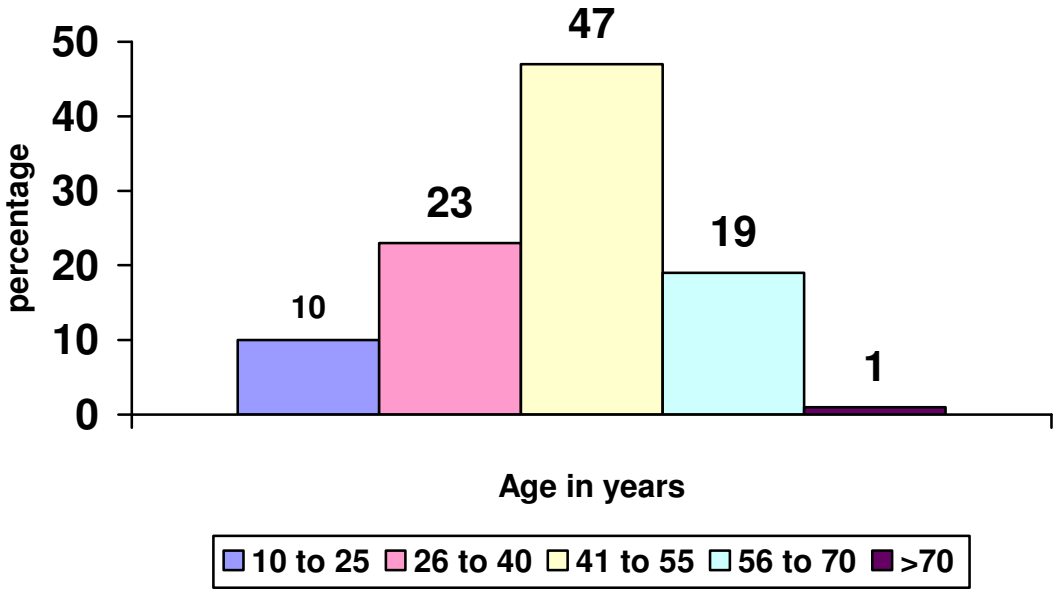
Sex distribution

Among the 70 patients 52 were males (74 %) and 18 were females (26%). Males: Females = 2.6**:**1 (Table 3 and figure16)

TABLE 3: SEX DISTRIBUTION

Sex	No. of Cases	Percent
Male	52	74%
Female	18	26%
Total	70	100%

Figure 15: Age distribution



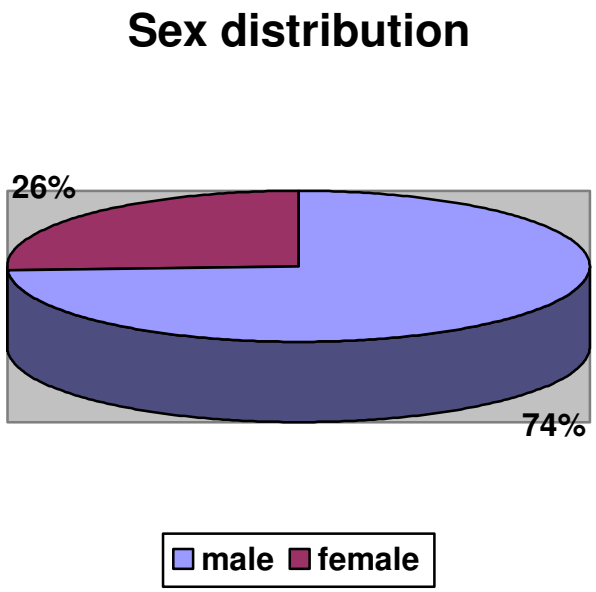


Figure 16

Vertigo

Of the 70 patients, 55 (79%) had typical surrounding rotatory type of vertigo. 15 patients (21%) had head rotating vertigo.

Among the 15 with head rotatory vertigo without the illusion of movement of surrounding, 9 (17%) had definitive Meniere's disease and 6 patients had possible Meniere's disease.

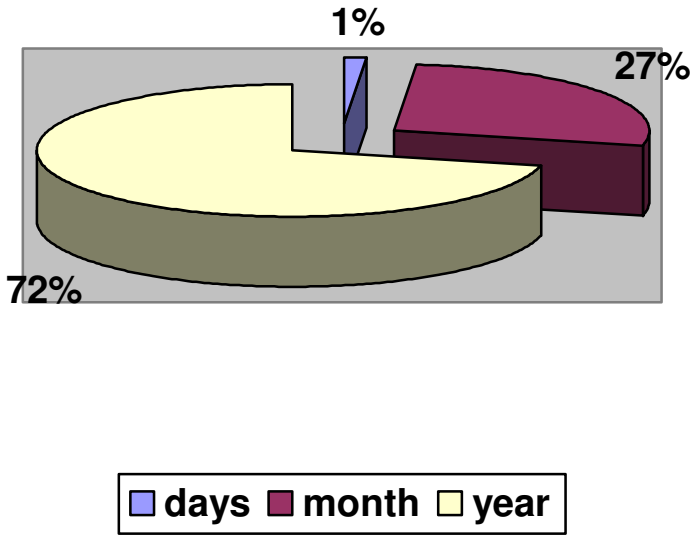
Total duration of vertigo

Of the 70 patients, 50 (71%) had vertigo for more than 1 year and 19 patients (27%) had vertigo less than a year (Table 4 and figure 17)

TABLE 4: TOTAL DURATION OF VERTIGO

Duration	No. of Cases	Percent
Days	1	2%
Months	19	27%
Years	50	71%
Total	70	100%

Figure 17: Total duration of vertigo



Duration of each attack of vertigo

Among the 70 patients, 20 (29%) had vertigo that last just minutes; 49 (70%) had vertigo lasting between 2 -3 hours and 10 with possible Meniere's patients also had vertigo durations between 2 -3 hours.

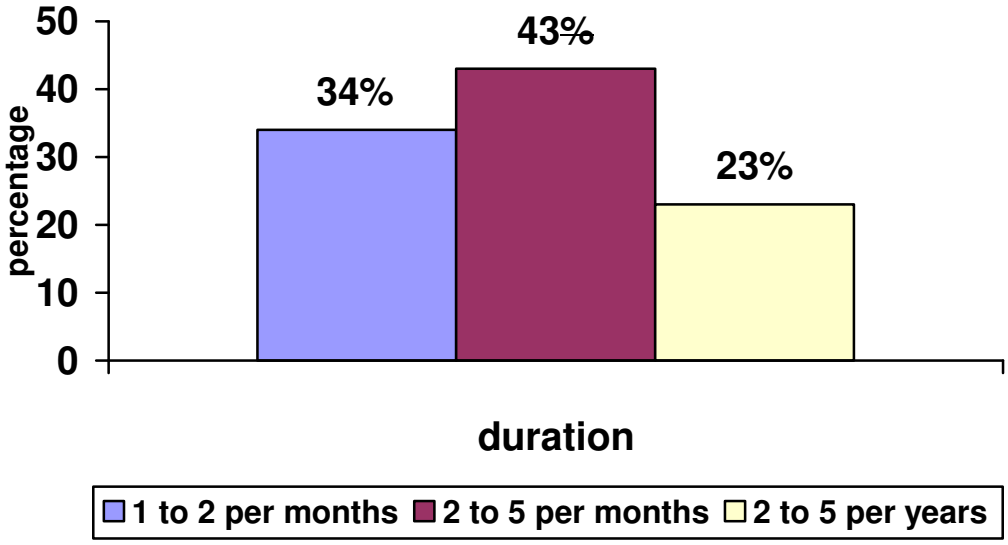
Frequency of attacks

Of the 70 patients, 24 (34%) had less than 2 attacks per month, 30 (43%) had 2 to 5 attacks per month and 16 (23%) had 2 to 5 attacks per year (Table 5 and figure18)

TABLE 5: FREQUENCY OF VERTIGO ATTACK

No of attack	No. of Cases	Percentage
1-2/month	24	34%
2-5/months	30	43%
2-5/Years	16	23%
Total	70	100%

Figure 18: Frequency of vertigo attack



Warning symptoms

Only 27 patients (39%) had warning signs in the form of either increasing tinnitus or aural fullness before the vertigo attack. (Table 6)

TABLE 6: WARNING SYMPTOMS BEFORE VERTIGO

Warning symptoms	No. of cases	Percent
Yes	27	39%
No	43	61%
Total	70	100%

Hearing loss

Among the 70 patients, 59 (84%) had hearing loss as per history, 20 (29%) had hearing loss in the right ear alone, 22 (31%) had hearing loss in the left ear alone and 17 (24%) had history of bilateral hearing loss (Table7)

TABLE 7: HEARING LOSS

Hearing loss	No. of cases	Percent
No	11	16%
Right side	20	29%
Left side	22	31%
Bilateral	17	24%
Total	70	100%

Only 27 patients (45%) had a history of fluctuating hearing loss.

50% of definite group had fluctuating hearing loss. 44 patients (63%) had hearing loss duration of 2-3 years. 39 definite Meniere's patients had hearing loss duration of 2-3 years.

Among the patients who had hearing loss, 37 (53%) had a worsening of hearing in the course of their disease. 13 (19%) were status quo in hearing loss since its onset.

Aural fullness

Among the 70 patients, 50 patients (71%) had aural fullness. Right side and left side were equally involved (Table 8)

TABLE 8: AURAL FULLNESS

Aural fullness	No. of cases	Percent
Present	50	71%
Absent	20	29%
Total	70	100%

Among the 50 with aural fullness, 20 (40%) had typical ear fullness or pressure at the time of vertigo attack. Among the definite group 17 patients (32%) had intermittent aural fullness.

Tinnitus

Of the 70 patients, 61 (87%) had tinnitus, of whom 24 (34%) had it on the right side, 25 had (36%) on the left side and 12 (17%) had bilateral tinnitus (Table 9). 51 (96%) patients with definite Meniere's patients had tinnitus 41 patients out of 61 patients had tinnitus for more than 3 years.

TABLE 9: TINNITUS

Side	No. of cases	Percent
No tinnitus	9	13%
Right	24	34%
Left	25	36%
Bilateral	12	17%
Total	70	100%

Among the 61 patients who had tinnitus, 36 (59%) had high pitch tinnitus, 25 (41%) had low pitch tinnitus and 23 (38%) had increasing tinnitus during the vertigo attack.

Blood investigations

Among the 70 patients, 44 (63%) had normal Hemoglobin and 23 (33%) had low hemoglobin, 59 (84%) had normal sugar and 11 (16%) high elevated blood sugars, 59 (84%) had normal cholesterol and 11 (16%) had high cholesterol, 13 (19%) had high triglycerides, 10 (14%) had low HDL levels and 3 had high LDL levels (Table 10).

TABLE 10: BLOOD INVESTIGATIONS

Test	No. of cases	Percent
Low Hemoglobin	23	33%
High Blood sugar	11	16%
High Cholesterol	11	16%
High Triglycerides	13	19%
Low HDL	10	14%
High LDL	3	4%

One patient had high TSH level and 1 had low TSH level.

None of the patients had positive serology test for syphilis.

AUDIOVESTIBULAR INVESIGATIONS

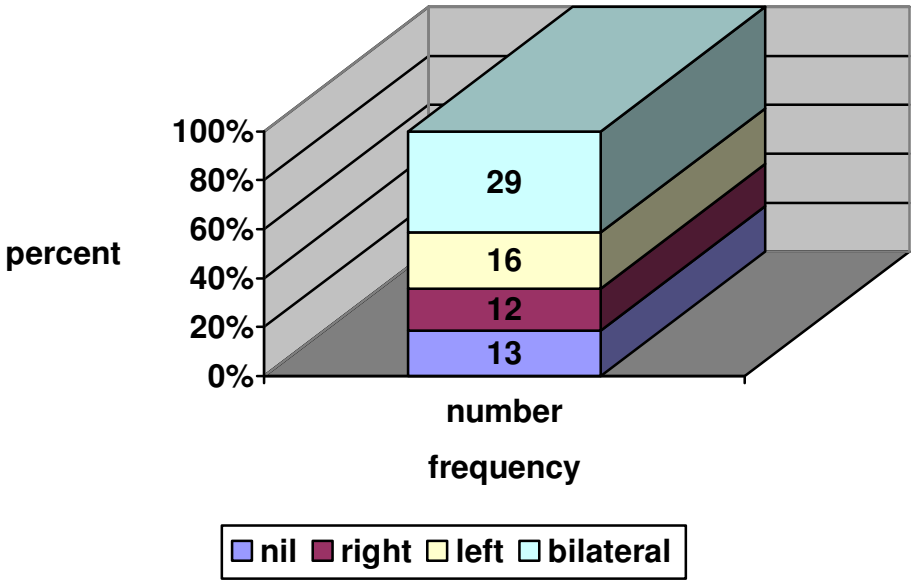
Pure Tone Audiometry

Among the 70 tested, 12 (17%) had hearing loss of the right ear, 16 (23%) had hearing loss of the left ear and 29 (41%) had bilateral hearing loss (Table 11and Fig19)

TABLE 11: PURE TONE HEARING LOSS

Side	No. of cases	Percent
Nil	13	19%
Right	12	17%
Left	16	23%
Bilateral	29	41%
Total	70	100%

Figure 19: Frequency of pure tone hearing loss



Pattern of pure tone audiogram

The pure tone audiometric pattern among the 57 patients as follows:

A flat pattern was most commonly noted 49% (n=28), down sloping was next most common 44% (n=25%) and least common type was up sloping 7% (n=4) (Table 12 and figure 20).

Figure 20: Pure tone audiogram pattern

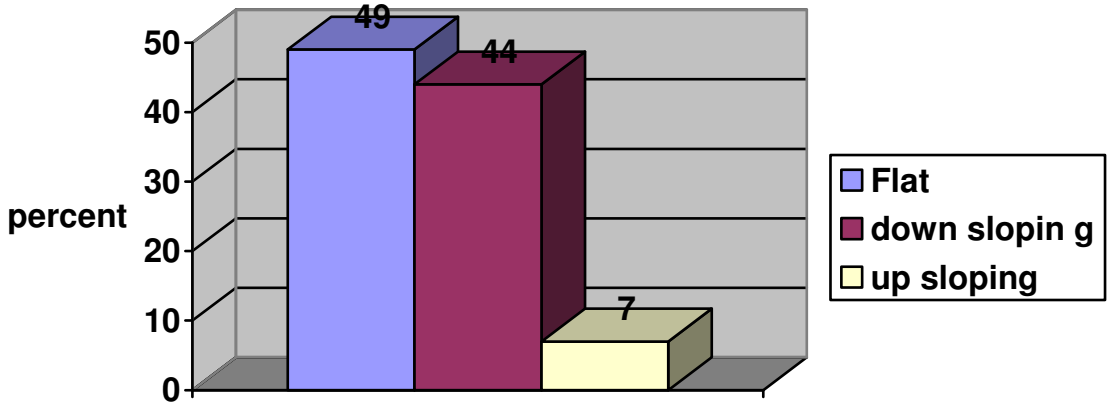


TABLE 12: PURE TONE AUDIOMETRY PATTERN

Pattern of PTA	No. of cases	Percent
Flat	28	49%
Down sloping	25	44%
Up sloping	4	7%
Total	57	100%

Glycerol Pure tone Audiometry test

Among the 57 with documented hearing loss, all had glycerol pure tone audiometry test. Positive glycerol test was noted in 25 cases (44%) (Table 13)

TABLE 13: GLYCEROL PURE TONE AUDIOMETRY

Test	No. of cases	Percent
Positive	25	44%
Negative	32	56%
Total	57	100%

Among the 53 definite Meniere's disease patients 25 patients (44%) had positive glycerol test. Among the 17 without definite Meniere's (3 probable + 14 possible) only 2 had glycerol test (as the others did not have hearing loss) and one had a positive glycerol test.

Impedance Audiometry

Of the 70 patients, 66 had type A Impedance curve; the rest (4) had C curve 85% patients had normal reflexes and 15% patients had Absent reflex (Table 14)

TABLE 14: IMPEDANCE AUDIOMETRY

Side	Right		Left	
Impedance	A curve	C curve	A curve	C curve
	66	4	65	5
Reflex	Present	Absent	Present	Absent
	59	11	60	10

Distortion product otoacoustic emission

Among the 70 patients, 60% (n=42) had absence of DPOAE and 40% (n=28) had normal DPOAE (Table 15). Among the definite group 14 patients had only right ear absent, 14 had absent in left ear and 27 had absent DPOAE in both ears.

TABLE 15: DISTORTION PRODUCT OTOACOUSTIC EMISSION

	No. of cases	Percent
Present	28	40%
Absent	42	60%
Total	70	100%

Electrocochleography

Among the 70 patients, 21 had (30%) unilateral abnormal ECohG and 39 had (57%) bilateral abnormal ECohG and 9 (13%) had normal ECohG (Table 16). Eight patients with possible Meniere's also showed bilateral abnormal ECohG, while 9 had normal ECohG.

TABLE 16: ELECTROCOCHLEOGRAPHY

	No. of cases	**Percent**
Normal	9	13%
Unilateral abnormal	21	30%
Bilateral abnormal	39	57%
Not done	1	0%
Total	70	100%

Positive predictive value for EcohG TEST

Among the 53 definite Meniere's disease patients, 52 patients had EcohG test (in 1 patient, the test was not done). Out of which, 45 patients (87%) had a positive EcohG test, 7 (13%) had negative test (Table 17). 14 (82%) patients out of 17 cases of probable & possible Meniere's had positive test.

TABLE 17: POSITIVE PREDICTIVE VALUE FOR EcohG TEST

ECohG test	Definite Meniere's	Not Definite Meniere's	Total
Positive	45	14	59
Negative	7	3	10
Total	52	17	69

The positive predictive value for ECohG test was calculated as:

a/a+b = 45/59 = 0.76 (i.e.) 76%

The negative predictive value for ECoG was calculated as d/c+d=3/10=0.3= 30%.

ECohG Distribution in various types of Meniere's disease

Among the 53 definite case, 45 cases (87%) had abnormal EcohG. In patients with probable disease all 3 had abnormal EcohG (Table 18).

TABLE 18: EcohG DISTRIBUTION IN VARIOUS TYPES OF MENIERE'S

	Meniere's disease					
	Definite	**percentage**	**Probable**	**percentage**	**possible**	**percentage**
Normal	7	13%	0	0%	3	21%
Abnormal	45	87%	3	100%	11	79%
Not done	1	0%	0	0	0	0
Total	53	100%	3	100%	14	100%

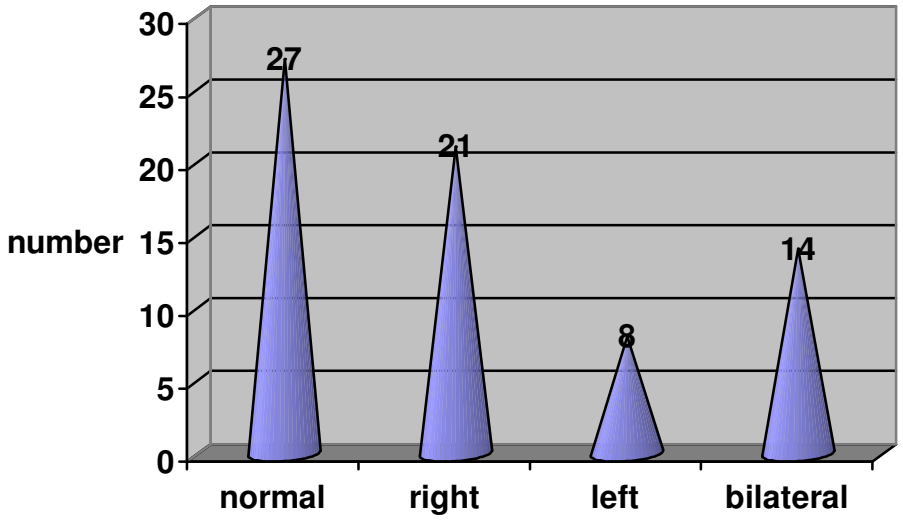
Electronystagmography

Total of 70 cases, 67 patients (95.7%) had normal smooth pursuit system.21 patients (30%) had right and 8 had (11%) left canal paresis and 14 patients (20%) had bilateral canal paresis. Among 14 bilateral canal paresis only 9 had definite Meniere's disease.16 patients had right directional preponderance (DP), 15 had left DP & 39 had no DP (Table 19 and figure 21).

TABLE 19: CANAL PARESIS

	No. of cases	Percent
Normal	27	39%
Right canal paresis	21	30%
Left Canal paresis	8	11%
Bilateral canal paresis	14	20%
Total	70	100%

Figure 21: Canal paresis



Stages of Definite Meniere's disease

Among the 53 definite Meniere's disease cases 31 Patients [8+10+13] (57%) were in Stage 3 and 8 Patients (15%) were in stage 4 (Table 20).

TABLE 20: STAGES OF MENIERE'S DISEASE (MD)

Stages of MD	Right	percent	Left	Percent	Bilateral	Percent
1 (<25dB)	1	2%	2	4%	3	6%
2 (26-40dB)	2	4%	2	4%	4	8%
3 (41-70dB)	8	15%	10	18%	13	24%
4 (>70dB)	1	2%	1	2%	6	11%

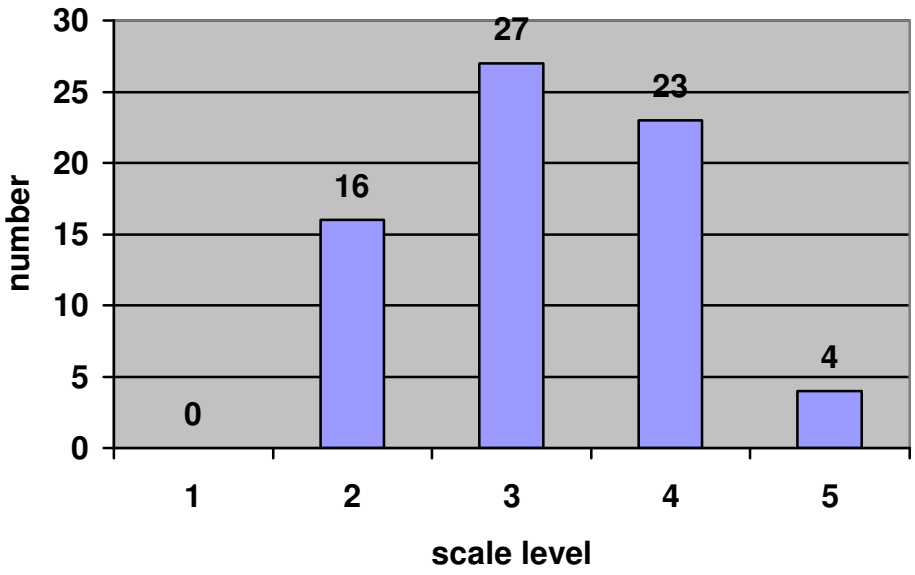
Functional Level Scale

Of the 70 patients, 27 (39%) were in functional level scale 3 and 23 were (32%) in level 4 (Table 21 and figure 22).

TABLE 21: FUNCTIONAL LEVEL SCALE OF MENIERE'S DISEASE

Level	No. of Cases	Percent
1	0	0%
2	16	23%
3	27	39%
4	23	32%
5	4	6%
Total	70	100%

Figure 22: Functional level scale



DISCUSSION

FREQUENCY OF MENIERE'S DISEASE

In the world literature the frequency of Meniere's is widely variable. The incidence of Meniere's disease ranging from 36 to 157[20, 21] per 100,000 in developed countries. There is no data published in peer reviewed journals showing the incidence or prevalence of Meniere's disease in a developing country like India. The present study found that the frequency of Meniere's disease in a tertiary level hospital is about 15.6%. However this hospital being tertiary centre, this does not reflect the extent of the problem among the general public.

In our study 53 patients (75.7%) had definitive Meniere's disease. 3 patients (4.3%) had probable Meniere's disease.14 patients (20%) had possible Meniere's disease. A larger case series may have detected more patients with probable and possible MD but this was not possible due to the time constraint for the study

AGE DISTRIBUTION

In the present study the patients ages ranged from 14 -70 years. Mean age for males was 45.84 years while mean age for females was 39 years. Mizukosh et al[55] study showed age distribution peaked at the age group of 40--49 years for males, while the peak for females was at the age group of 30--39 years[37.] This is well correlated with our study.

SEX

According to the available literature male female ratio is almost equal[22]. The study conducted by Wantanabe

[56] in Japan there is slight female preponderance. However in this study a male predominance was noted. This could be because it reflects the male/female attendance in our audio vestibular clinic which also has a male preponderance (2:1). In India, men seek medical attention more than women.

VERTIGO

Paparella & Mancini[57] described vertigo in about 91% of Meniere's patients. The typical Meniere's type of vertigo attack seen in our study was 79% (n=55). Remaining 21% presented with head rotatory vertigo without illusion of movement of surrounding. It is important to remember that Meniere's patients can present with either typical surrounding vertigo or just head rotatory vertigo.

Out of 70 patients, 50 patients (71%) had the total duration of vertigo more than 1 year. 84% had attacks more than 4 typical spells. The duration of each spell of vertiginous attack in this study was between 2-3 hours in 70% (n=49) of the patients. Other studies like Oosterveld et al[27] also showed most of the episodes lasting for 2-3 hours. Another study by Paparella et al[57]revealed that in 25% of patients, vertiginous attacks lasted less than I hour, 50% had 1-2 hours and only in 25 % more than 2 hours.

The frequency of vertiginous attacks in this study was much higher (43% patients showed 2-5 attacks per month) than other study (Paparella et al[57])

The above three findings indicate more prolonged and frequent attacks of Meniere's disease in our patients and this may be due the referral pattern in this specialized tertiary care centre. This may not be representative of the disease in general population at large.

HEARING LOSS

In our study 81% patients had hearing loss. 29% had right ear hearing loss, 31% left ear and 24% had bilateral hearing loss. Mari Havia et al[58] study showed right side involvement in 38%, left sided in 46% & bilateral in 16%.This side prediction correlates with our study in which left ear is more commonly involved. The reason behind this side prediction is not known.

Paparella (1984) study[59] indicates the hearing loss is typically fluctuating. The present study we found 45 % of patients had fluctuation in their hearing loss.

According to Enander[60] hearing deteriorates in first year of disease, thereafter stabilization occurs. But in our study more than half (53%) the patients had progressively worsening hearing even though they have been suffering from the disease for many years.

Aural fullness

Paparella study[25] shows aural fullness in Meniere's disease is 74.1%. In our study 71% patients had aural fullness with worsening symptoms during the attacks in 42%.

Tinnitus

The tinnitus in Meniere's disease is typically described as low pitched[31].However in our study high pitch tinnitus was more common than low pitched tinnitus.

INVESTIGATIONS

Hemoglobin

33% patients had low hemoglobin which may be attributed to the nutritional deficiency of our country. No article indicates any correlation between low Hb and Meniere's disease.

Blood sugar levels and dyslipedimia

Both were found to be elevated in 15% of cases. As described by Haid et al[61] these may be co-morbid factors may be related to the concurrent age factors of these patients.

Pure Tone Audiometry: Audiogram pattern

Mayerhof et al[35] study reveals the audiogram pattern were flat in 42%, rising in 7%, peaked in 32%, and sloping downward in the remaining 19%.This observation is correlating with our study where the flat type was most common (49%) however the peak type of audiometric pattern was not seen in our patients.

Glycerol pure tone audiometry

Study done by Akoika et al[40]found that 47% patients had positive glycerol test in their series. Our study showed 44% positive glycerol test. This is well correlated with the other study.

Positive predictive value for glycerol test in various types of Meniere's disease was attempted**.** A comparative positive predictive value could not be done due to the small numbers who had the glycerol test in this group.

Impedance Audiometry

The literature shows[36] about 33% of Meniere's disease had low middle ear pressure, but in our study only 7% had low middle ear pressure revealed as C type curve. Acoustic reflex was absent in patient with stage 4 disease only where the hearing loss is much high (>70dB).

Distortion product otoacoustic emission

In this study 60% of patients had absence of DPOAE which was similar to the study by Cianfrone et al[62].

Electrocochleography

Study by Gibson et al[63] found enlarged SP:AP in 62-78% of patient's with Meniere's disease. Another study by Chung et al[64] found sensitivity and specificity of extra tympanic electrocochleography in the diagnosis of Meniere's disease to be 71% and 96%, respectively. The positive predictive value for ECohG in our study was 76%. But this test has low negative predictive value of 30%.

Electronystagmography

Dobie RA et al[52]reported ENG findings in Meniere's disease. He found spontaneous and/or positional nystagmus (SN, PN) in 32% of patients. unilateral caloric weakness (UW) in 49%, directional preponderance (DP) in 36%, and Bilateral caloric weakness (BW) occurred in 36% of patients with bilateral hearing loss. ENG was reported as normal in 25%.

In our study 77% had spontaneous or induced nystagmus which is much more than the above study. This trend of seen both in caloric weakness and directional preponderance as compared to other studies.

Staging for definitive Meniere's disease

Most common stage in our patients presenting to us in stage 3 (57%) where patient had 41-70dB hearing loss. The next common stage is stage 4 (15%). This may indicate late referrals to the clinics by primary or secondary care physicians or late seeking of medical attention by the patients in our country.

Functional Level Scale

Most common level is 3 (38.6%) and second most common in level 4 (32.9%) which definitely influence the daily activity of the patient. Early diagnosis and treatment of this condition gives the near normal life & prevent further progression of the disease.

CONCLUSIONS

- Frequency of Meniere's disease according to AAO criteria is about 15.6% in the tertiary care audio vestibular center.
- It was found more commonly in males than females (2.6:1)
- The highest frequency was seen in the age group 40-49 in males and 30-39 years in females.
- Frequency of vertigo attacks more common in this study group (2-5 attacks per month).
- Left ear is more commonly affected in this study.
- High frequency tinnitus is more common than low frequency in this study.
- Glycerol pure tone audiometry may be a useful test in the diagnosis of the condition.
- Impedance audiometry does not influence the diagnosis.
- Extratympanic Electrocochleogram supports the evidence of endolymphatic hydrops with the positive predictive value of 76%.
- ENG demonstrates the canal paresis & pattern of nystagmus.
- Indian patients more commonly in the functional level scale of 3.
- Definite cases of Meniere’s disease presented in stage 3.

BIBILIOGRAPHY

1. Schessel D.A, Nedzelski. Meniere's disease and other peripheral vestibular disorders. Otolaryngology, Head and Neck surgery. Mosby. 1993; 2nd edition: 3152-3176.
2. Pfalz C.R, Thomsen. Symptomatology and definitions of Meniere's disease. Controversial aspect of Meniere's disease. edited by C.R Pfalz. 88-95
3. Committee on Hearing and Equilibrium adopted by the Board Directors of the American Academy of Otolaryngology- Head and Neck surgery, March12,1994. Otolaryngology-Head and Neck surgery. 1995; Vol 113: 3: 181-185.
4.. Sady Costa. Meniere's disease- overview, epidemiology, and natural history. Otolaryngology Clinics North America. 2002; Vol 35: 455.
5. David A, Moffat, Robert H, Ballagh. Meniere's Disease. Scott Brown's Otolaryngology. Butterworth Heinemann. 1997; 6th edition. Vol 3: 19
6. Lawrence R Lustig, Anil Lalwani. History of Meniere's disease. Otolaryngol Clin N Am. 1997; Vol 30: 929
7. Pappas DG. Barany's History of Vestibular physiology Translation and Commentary. Ann Otol Rhinol Laryngol. 1984; 110:1-16
8. Lawrence R Lustig, Anil Lalwani. History of Meniere's disease. Otolaryngol Clin N Am. 1997; Vol 30: 930

9. Baloh RW. Robert Barany and the controversy surrounding his discovery of the caloric reaction .Neurology. 2002; 58 (7):1094-9.

10. Peter Savundra, Linda. The physiology of equilibrium and its application to the dizzy patient. Scott-Brown's Otolaryngology. Edited by Michael Gleeson.1997: 6th Edition. Vol 1: 4: 1-5

11. Lim. D.J. The development and the structure of otoconia. Ultra structural Atlas of the Inner ear, edited by Friedman and J. Ballantyne. London. Butterworths. 1993; 245-269

12. Norma B. Slepecky. Ultrastructure of the inner ear. Pathology of the Ear edited by I. Friedmann and W. Arnold. Churchil Livingstone publications. 451-459

13. Applied Anatomy. Mawson's Disease of the ear. Edited by Harold Ludman 1988; Fifth Edition. 17-73

14. Leigh R, Zee D. The Neurology of Eye movements. Philadelphia, FA Davis 3rd edition 1999;

15. Neile T, Sheperd, David Solomon. Functional operation of the balance system in daily activities. Otolaryngologic clinics of North America 2000; Vol 33 3:455-69.

16. Alford B.R .Meniere's disease. Criteria for diagnosis and evaluation of therapy for reporting. Report of subcommittee on equilibrium and its management. Transactions of the American Academy of Ophthalmology and Otolaryngology 76:1462-1464.

17. David A Moffat, Robert H Ballagh. Meniere's Disease. Scott Brown's Otolaryngology. Edited by John B. Booth 1997; 6th edition: Vol 3: 19: 2

18. Moffat D, Booth, and Morrisson A.W. Metabolic investigations in Meniere's disease. Preliminary findings. J Laryngol Otol.1979; 93 (6): 545-61.

19. Brown DH, McClure JA, Downar Zapolski Z. The membrane rupture theory of Meniere's disease--is it valid?. Laryngoscope. 1988;98: 599-601.

20. Shojaku et al. The prevalence of definite cases of Meniere's disease in the Hida and Nhikubiki districts of central Japan. A survey of relatively isolated areas of medical care. Acta Otolaryngol suppl.1997; 528:94-6

21. Cawthrone T, Hewlett. Meniere's disease .Proceedings of the Royal Society of Medicine. 1954; 47: 663-670

22. Mizukoshi K, Watanabe et al. Epidemiological survey of definite cases of Meniere's disease collected by the seventeen members of the Meniere's Disease Research Committee of Japan in 1975--1976I. Adv Otorhinolaryngol. 1979; 25: 106-11.

23. David A. Moffat , Robert H. Ballagh. Meniere's Disease .Scott Brown's Otolaryngology. Edited by John B. Booth. 1997; 6th edn: Vol 3:19 3-4

24. House JW, Doherty JK, Fisher LM, Derebery MJ, Berliner KI. Meniere's disease: prevalence of contralateral ear involvement. Otol Neurotol. 2006; 27 (3): 355-61.

25. Paparella M.M, Mancini. Vestibular Meniere's disease. Otolaryngol Head Neck Surg. 1985; 93(2):148-51

26. Barber H.O. Meniere's Disease: Symptomatology .A Comprehensive Appraisal edi by W.J. Oosterveld. New York. John Wiley. 1983; 25-34.

27. Oosterveld W.J. Meniere's disease, signs and symptoms. J Laryngol Otol. 1980; 94(8):885-92.

28. Friberg, Stahle J, Svedberg. The natural course of Meniere's disease Acta Otolaryngol Suppl. 1984; 406:72-7.

29. Committee on Hearing and Equilibrium Adopted by the Board Directors of the American Academy of Otolaryngology- Head and Neck surgery, March12,1994. Otolaryngology-Head and Neck surgery 1995; Vol 113: 3: 181-185

30. Greven AJ, Oosterveld WJ. The contralateral ear in Meniere's disease Arch Otolaryngol. 1975;101 (10): 608-12

31. Herraiz C, Tapia MC, Plaza G. Tinnitus and Meniere's disease: characteristics and prognosis in a tinnitus clinic sample .Eur Arch Otorhinolaryngol. 2006; 263 (6): 504-9

32. Paparella M.M, Mancini F. Vestibular Meniere's disease. Otolaryngol Head Neck Surg. 1985; 93(2):148-51

33. Committee on Hearing and Equilibrium Adopted by the Board Directors of the American Academy of Otolaryngology-Head and Neck surgery, March12,1994. Otolaryngol-Head and Neck surgery 1995;181-185

34. Alexander et al. Diagnostic Testing for Endolymphatic Hydrops. Otolaryngol Clin N America 1997; Vol 30: 6: 987-1002

35. Meyerhoff WL, Paparella MM, Gudbrandsson FK. Clinical evaluation of Meniere's disease. Laryngoscope.1981;91(10):1663-8.

36. Morinaka S, Nakamura H. Middle ear pressure in patients with dizziness. Ann Otol Rhinol Laryngol. 2004; 113(11):906-13.

37. Klockhoff and Lindblom. Endolymphatic hydrops revealed by glycerol test : preliminary report. Acta Otolaryngol 1966;61:459-461

38. Klockhoff and Lindblom. Glycerol test in Meniere's disease. Acta Otolaryngol Suppl 224;449-451.

39. Serge Padoan. Oral Versus IV administration of the Glycerol test: Side effects and Usefulness. Acta Otolaryngol 2003;123:482-487

40. Akoika, A. Fugita et al: A clinical study of the diagnosis of the Endolymphatic aspects of Meniere's disease. Meniere's disease.Springer-Verlag,1990, 125-132.

41. Snyder JM: Extensive use of a diagnostic test for Meniere's disease. Arch Otolaryngol 1974;100:360-365

42. Anirban Biswas. Clinical Audio-Vestibulometry for Otologist and Neurologists 2002; Third Edition. 5:91

43. Probst R, Lonsbury MB et al: A review of otoacoustic emission J Acoust Soc Am .1991; 89:2027-2067

44. Harris FP Probst R. Transiently evoked and distortion-product otoacoustic emissions in patient with Meniere's disease. Acta Otolaryngol 1992;112:36-44

45. Committee on Hearing and Equilibrium. Report of Subcommittee on Equilibrium and its Measurement. Meniere's disease: criteria for diagnosis and evaluation of therapy for reporting. Trans Am Acad Ophthalmol Otolaryngol 1972;76(6):1462-64

46. Mori N, Asai H, Doi K, Matsunaga T. Diagnostic value of extra tympanic electrocochleography in Meniere's disease. Audiol 1987;26 (2):103-10.

47. Coats A, Dickey J. Nonsurgical recording of human auditory nerve action potentials and cochlear microphonics. Ann Otol Rhinol Laryngol 1970;79:844-51

48. Aso S, Watanabe Y, Mizukoshi K.A clinical study of electrocochleography in Meniere's disease. Acta Otolaryngol. 1991;111(1):44-52

49. Orchik DJ, Shea JJ, Ge NN. Summating potential and action potential ratio in Meniere's disease before and after treatment. Am J Otol 1998; 19:478–83

50. Pappas, Dennis Extratympanic Electrocochleography: Diagnostic and Predictive Value American Journal of Otology Vol 21(1), 2000; 81-87

51. Anirban Biswas. Clinical Audio-Vestibulometry for Otologist and Neurologists 2002; 3rd Edition: 7:135

52. Dobie et al. Electronystagmographic and audiologic findings in patients with Meniere's disease Acta Otolaryngol July-Aug;94(1-2):19-27

53. Maureen Valente. Audiometric tests, In Practical management of Dizzy patients, edited by Joel A,Goebel, Lippincott Williams and Wilkins Philadelphia, 2001; 15:171-184

54. Levine S, Margolis RH, Daly KA ."Use of electrocochleography in the diagnosis of Meniere's disease." Laryngoscope 1998; 108(7):993-1000.

55. Mizukoshi K Ino H, Ishikawa K, Watanabe Y, Yamazaki H, Kato I, Okubo J, Watanabe Epidemiological survey of definite cases of Meniere's disease collected by the seventeen members of the Meniere's Disease Research Committee of Japan in 1975--1976I Adv Otorhinolaryngol. 1979; 25:106-11.

56. Watanabe et al Epidemiological and clinical characteristics of Meniere's disease in Japan. Acta Otolaryngol Suppl. 1995; 519:206-10

57. Paparella MM, Mancini F, Liston SL. Otosclerosis and Meniere's syndrome: diagnosis and treatment. Laryngoscope. 1984 ;94:1414-7

58. Mari Havia, Erna Kentala. Progression of Symptoms of Dizziness in Menieres disease. Arch Otolaryngol Head Neck Sur. 2004;130:431-435

59. Paparella MM. Pathogenesis of Meniere's disease and Meniere's syndrome. Acta Otolaryngol Suppl. 1984; 406:10-25

60. Enander A, et al. Hearing in Meniere's disease. A study of pure-tone audiograms in 334 patients Acta Otolaryngol 1967; 64(5):543-56.

61. Haid CT, Watermeier D, Wolf SR, Berg M. Clinical survey of Meniere's disease: 574 cases.Acta Otolaryngol Suppl. 1995;520: 251-5

62. Cianfrone G, Ralli G, Fabbricatore M, Altissimi G, Nola G. Distortion product otoacoustic emissions in Meniere's disease, Scand Audiol. 2000;29(2):111-9

63. Gibson WPR, Moffat DA, Ramsden RT. Clinical electrocochleography in the diagnosis and management of Meniere's disorder. Audiology 1977;16:389–401

64. Chung WH, Cho DY, Choi JY, Hong SH. Clinical usefulness of extratympanic electrocochleography in the diagnosis of Meniere's disease. Otol Neurotol. 2004;25(2):144-9.

Annexure 1
Vertigo clinic evaluation form

Name **Age** **Sex** **Hospital no**

Presenting complaint: vertigo /lightheadedness / imbalance /others_____

1. **VERTIGO (**An illusion of movement (Rotatory /linear displacement)

Duration of vertigo hours days months years

Description of first attack:

Mode of onset: sudden/gradual;

Duration seconds minutes hours days

Was the first attack worst: yes/ no /same as other attacks

Precipitating factors: nil/coughing/sneezing/loud sounds/specific food/ specific head positions/Standing from sitting position/turning in bed /raising hands/ others

Associated with: nil / nausea/vomiting / tinnitus/hearing loss/ blurring of vision/ slurring of speech/ headache / photophobia / phonophobia/others:

Subsequent attacks

Progression: downhill / improving / episodic / progressive / status quo

Type of vertigo: episodic continuous uncertain

Present at rest at rest and movement on movement only

Head rotating surrounding rotating uncertain

Duration of each attack: Seconds / hours / days / weeks

Date of last attack **Frequency of each attack**

Periods in between attacks free of symptoms not free of symptoms

Warning signs before attack nil / fullness in ear / aura / others

Clustering of attacks yes no

Fullness/pressure sensation in the ear yes no

Tinnitus nil / rt (yes / no)left (yes / no) annoyance / continuous / intermittent

Hearing loss: nil rt (yes / no) left(yes / no) fluctuating (rt / left)/

phonophobia; better/ worse in noisy surroundings/ rapidly progressing

hearing loss/ sudden in onset

Aggravating/precipitating factors: nil / coughing/sneezing/loud sounds/specific

Relieving factors nil /yes (specify)

Vegetative symptoms (nausea/vomiting/sweating/others) yes no

Positional vertigo yes/no **drop attacks** yes/no **Oscillopsia** yes/no

Motion sickness yes no **Acoustic trauma** yes no

Difficulty walking in the dark/streets/open spaces yes no

Any URI/fever before attack yes no **Any barotrauma** (swim/fly)

Other ENT complaints yes no (ear discharge ,others

Neurological complaints yes no (dysarthria / diplopia/ headache/ loc /

blackouts / pins and needles or tingles in hand and feet / facial pain or numbness

/ spots before eyes/ seizures / others)

Headache: no yes severity (mild / moderate / severe; side: site:

associated nausea /vomiting / scotomas /aura / others

Cervical pain no yes **Loss of balance on walking** no yes

Cardiovascular disorders no yes (hypertension / past h/o MI/palpitations/

chest pain/leg pain on walking or at rest / CCF /other

Medical problems no/ yes (thyroid / DM / anemia /polycythemia/ autoimmune/

TB / smoking /alcohol / /loss of wt / appetite / blood in stools /diarrhea / food

intolerance/ indigestion / bleeding disorders /macroglobinaemia/ others)

Eye problems no/yes(loss of vision /pain /discharge or tearing /

glaucoma/ diplopia/ refractory errors/new glasses/others)

Head injury/ any trauma no yes

Ototoxic /other medications no/yes(Immunosuppressant/steroids/others)

Psychiatric no yes (Insomnia / depression / conversion reactions/ agro phobia

Any known allergy no yes

Family h/o giddiness/Psych disturbance no yes

Time off work/school

2. **NEAR FAINT**-Sensation of impending faint (light headedness)

Orthostatic hypotension- reduced blood volume, hypotensive drugs,

Vasovagal attack- prolonged standing in hot sun, fear**,** acute vertigo

Hyperventilation- anxiety, stress, panic attacks

Decreased cardiac output –arrhythmia, valvular disease, heart failure

Postural hypotension no yes **hypotensive drugs** no yes

Antidepressants no yes major tranquilizers no yes

Any h/o autonomic dysfunction no yes

(Bladder / bowel dysfunction/ peripheral neuropathy)

H/o Vasovagal attack no yes

H/s hyperventilation no yes

H/so reduced cardiac output no yes(Arrhythmia / valvular disease/ccf)

3. PSYCHOPHYSIOLOGICAL DIZZINESS - Sensation of floating/swimming)

Associated with tension headache /palpitations / fatigue / weakness no yes

PHYSIOLOGICAL OVERLOAD

Any h/o air travel/sea travel no yes H/o motion sickness no yes

NEURO-OTOLOGICAL EXAMINATION

Systemic **Pallor** y / n **BP** lying standing

Bruits carotids no / yes rt / lft

Peripheral pulses dorsalis rt/lft radial rt/lft

Ears **TM** rt lft

TFT **Rennie** rt lft **Webers** rt lft **ABC** rt lft

Cranial nerves **corneal** rt lft

Eye movements normal /abnormal **ptosis** no yes

7th **9th** **10th** **11th** **12th**

deep tendon reflexes normal /abnormal **Babinsky** normal /abnormal

muscle strength normal /abnormal **sensation** -**face** normal /abnormal

Cerebellar functions **Finger to nose eyes open** **eyes closed**

EXAMINATION OF BALANCE SYSTEM

1) VESTIBULOSPINAL

STATIC IMBALANCE

Romberg's **standing test** **Walking-tandem**

eyes open eyes closed eyes open eyes closed eyes open eyes closed

EXAMINATION OF GAIT

2) VESTIBULO-OCCULAR SYSTEM ABNORMAL EYE MOVEMENTS

Opsoclonus yes no **ocular bobbing** yes no **ocular flutter** yes no

Inspection of spontaneous nystagmus

Using Frenzel Lens no / yes

(Without optic fixation)jerky/ pendular direction changing /direction fixed

Without Frenzel lens no/yes horiz (rt/ lft) rotat

Skew deviation and ocular tilt reaction

The alternate cover test/Madrox rod **horiz** no / yes **vertical** no / yes

Saccades no/yes **Smooth pursuit** normal / abnormal

Head shaking nystagmus no yes (horizontal rt/lef vertical no / yes)

Head -thrust test *no* *yes rt / lft*

Positioning testing ***Dix- Hallpike maneuver***

.

Positional nystagmus sitting **supine**

Dynamic visual nystagmus no yes **Valsalva induced nystagmus** no yes

Hyperventilation dizziness no yes **nystagmus** no yes

Tullio phenomenon no yes **Fistula test** no yes

Vestibular exercises

Annexure 2

MENIERE'S DISEASE PROFORMA

Name:

Sex :[1] male,[2]female **Age** [1]10-25,[2]26-40,[3]41-55,[4]56-70,[5]>70

Hospital no:

Date:

Dizziness [1] Yes/ [2]No

Character [1] Rotatory /[2] Imbalance

Vertigo Type: [1] Head rotating [2] Surrounding rotating

Total duration: [1] Days [2] Months [3] Years

Number of episodes: [1]< 2 [2] 2-4 [3] >4

Each episode duration: [1]Min [2] Hours [3] Days

Frequency of attack: [1]<2 /month [2]2-5/month [1-2]/ year

Warning signs before attack: [1]Yes /[2] No

Hearing loss [1]Yes /[2] No

Side [1] rt only [2] left only [3] Bilateral

Fluctuating [1]Yes /[2] No

Duration [1] Days [2] Months [3] Years

Onset: [1] Insidious /[2] sudden

Progression: [1] Improved /[2] worst / [3]status quo

Aural fullness / Pressure [1]Yes /[2] No

Side [1] rt only [2] left only [3] Bilateral

Duration [1] Days [2] Months [3] Years

Character [1]Continuous [2]intermittent 3]at vertigo attack

Tinnitus [1]Yes /[2] No

Side [1] rt only [2] left only [3] Bilateral

Duration [1] Days [2] Months [3] Years

Pitch [1]High pitch/[2]low pitch

Character [1]Continuous [2]Intermittent [3]at vertigo attack

Secondary causes

Head trauma [1]Yes /[2] No

Post Infective [1]Yes /[2] No

Autoimmune [1]Yes /[2] No

H/o previous hearing loss [1]Yes /[2] No

INVESTIGATIONS

Hb: [1]12-16 f,13.5-18 m.[2]<12 f,<13.5 m [3]>14f, >18 m

PC [1]80-140,[2] >140,RBS[1]60-160[2]>160

Lipid profile: Serum cholesterol[1]<200 [2]>200,Triglycerides[1]45-190 [2]>190 HDL[1]35-70 [2]>70,[3]<35. LDL[1]<160 [2]>160

TSH [1] 0.3-4.5 [2] >4.5 [3] <0.3

TPHA 1 [positive] 2[negative]

PTA [1] <25dB,[2]26-40,[3]41-70,[4]>70 Right Left

Preglycerol (Average of 0.5,1,2 & 3 kH)

Post glycerol [1]yes,[2]no

Impedance

Curves 1[A] 2[B] 3[C] 4[D] 1[A] 2[B] 3[C] 4[D]

Reflexes [1]present [2]absent [1]present [2]absent

DPOAE: [1]present[2]absent [1]present [2]absent

Electrocochleography: [1]normal [2]abnormal [1]normal [2]abnormal

ENG: Nystagmus:[1] present [2] absent [1] present [2] [absent

Caloric:[1]normal [2] R canal paresis[3] left canal paresis[4]bilateral c.p

Directional preponderance [1]Right DP [1] left DP

DIAGNOSIS:

[1] **Definitive** (2 or more definite vertigo with documented hearing loss, tinnitus or aural fullness in treated ears)

[2**]Probable** (1definitive episode of vertigo, documented hearing loss, tinnitus or aural fullness in treated ears)

[3]**Possible**(Episodic vertigo of Meniere's type without documented hearing loss, or sensorineural hearing loss, or SN loss, fluctuating or fixed, with disequilibrium but without definitive episodes)

STAGE (For definite cases only)

PTA thresholds average at 0.5,1,2& 3kHz	[1] <25dB	[1] <25dB
	[2] 26-40dB	[2] 26-40dB
	[3] 41-70dB	[3] 41-70dB
	[4] >70dB	[4] >70dB

FUNCTIONAL LEVEL SCALE 1 2 3 4 5 6

KEY TO THE MASTER CHART

Name

Age 1]10 to 25 years,2]26 to 40 years, 3] 41 to 55 years,

4] 56 to 70 years 5] > 70 years

Sex 1-male 2- female

v t –vertigo type 1] head rotating, 2]surrounding rotating

td--total duration 1]-days,2-months,duration,

no.epi--number of episode, 1]>2,2] 2-4,3]>4

epi d–episode duration 1]in minutes,2]hours, 3]days,

f a-Frequency of att [1]<2 /month [2]2-5/month [1-2]/ year

w s- warning symptoms[1]Yes /[2] No

hl- Hearing loss [1]Yes /[2] No. hls-- Side [1] rt only [2] left only [3] Bilateral

hlf -- Fluctuating [1]Yes /[2] No. hl dur--Duration [1] Days 2] Months [3] Years

hlp Progression: [1] Improved /[2] worst / [3]status quo

af -- Aural fullness / Pressure [1]Yes /[2] No

afc--Character [1]Continuous [2]intermittent 3]at vertigo attack

ti Tinnitus [1]Yes /[2] No tis-- Side [1] rt only [2] left only [3] Bilateral

tis d Duration [1] Days [2] Month [3] Years tip -- Pitch [1]High pitch/[2]low

tic-- Character [1]Continuous [2]Intermittent [3]at vertigo

hb Hb: [1]12-16 f,13.5-18 m.[2]<12 f,<13.5 m [3]>14f, >18 m

sugar Blood sugar level (post prondial) PC [1]80-140,[2] >140

cho Serum cholesterol[1]<200 [2]>200, tg-Triglycerides[1]45-190 [2]>190

hdl-HDL [1]35-70 [2]>70,[3]<35. ldl-- LDL[1]<160 [2]>160

Pta pure tone audiogram 0] no hearing loss,1] right hearing loss,3] left hearing loss, 3] bilateral hearing loss.

gly—glycerol pure tone audiometry 0]no,1]positive, 2] negative

im r Impedance Curves right 1[A] 2[B] 3[C] 4[D] im lt Impe left side 1[A] 2[B] 3[C] 4[D] im r Reflex [1]present [2]absent im lt Reflex [1]present [2]absent

dpoae DPOAE: [1]present[2]absent

Ecohg Electrocochleography:0] not done [1]normal [2]unilateral abnormal 3]bilateral abnormal

sp n s Nystagmus:[1] right beating [2] left beating,3] nil

Cal Caloric:[1]normal [2] R canal paresis[3] left canal paresis[4]bilateral

Dp Directional preponderance [1]Right DP [1] left DP

Men s r Meniere's stage right side [1] <25dB [2] 26-40dB [3] 41-70dB [4] >70

Mens l Meniere's stageleft side [1] <25dB [2] 26-40dB [3] 41-70dB [4] >70

Men s b/l Meniere's stage bilateral [1] <25dB [2] 26-40dB [3] 41-70dB [4] >70

fls FUNCTIONAL LEVEL SCALE 1 2 3 4 5 6

S.NO	hosp no	age	sex	vt	td	no epi	epi dur	fr att	ws	hl	hls	hlf	hld	hlp	af	afs	afc	ti	tis	tisd	tip	tic	Hb
1	195773B	2	1	1	3	3	3	1	2	1	1	2	3	2	2	0	0	1	1	3	2	2	3
2	311962B	3	2	2	3	3	2	3	2	1	3	2	3	2	1	3	2	1	3	3	1	2	3
3	318168C	4	1	2	3	3	2	1	1	1	2	2	3	1	2	0	0	1	2	3	1	3	1
4	446561C	3	1	2	3	3	2	1	1	1	2	2	3	2	1	2	1	1	2	3	2	3	1
5	461600C	1	2	2	3	3	1	2	2	1	2	2	3	2	2	0	0	2	0	0	0	0	2
6	468748C	3	1	2	3	3	2	1	2	1	3	1	3	1	1	1	3	1	1	3	1	1	1
7	479575C	4	1	2	3	3	2	2	1	1	1	2	3	2	1	1	3	1	1	3	1	2	2
8	571861C	4	1	2	3	3	2	1	2	1	3	1	3	2	1	1	2	1	3	2	2	2	2
9	598353C	2	1	2	3	3	2	1	1	2	0	0	0	0	1	2	3	1	2	3	2	3	1
10	680968C	3	2	2	2	1	2	2	2	1	1	1	2	2	2	0	0	1	1	2	1	1	1
11	694728C	3	1	2	3	3	2	1	2	1	3	1	3	2	1	3	2	1	3	3	1	3	1
12	706867C	3	2	2	3	3	2	1	1	2	0	0	0	0	2	0	0	2	0	0	0	0	1
13	709035C	3	1	2	2	1	2	1	1	1	2	2	3	2	1	2	2	1	2	3	1	1	1
14	713459C	3	1	1	3	3	1	3	2	2	0	0	0	0	2	0	0	1	2	1	2	2	1
15	729436C	3	1	2	2	1	2	1	1	2	0	0	0	0	1	3	2	1	2	2	2	2	1
16	730605C	4	1	2	2	3	2	1	2	1	1	2	2	3	2	0	0	1	1	2	1	2	1
17	731311C	4	1	2	3	3	2	2	2	1	2	2	3	2	1	2	3	1	2	2	1	1	2
18	733099C	2	1	2	3	3	2	1	2	1	2	1	3	2	1	2	2	1	1	3	2	2	2
19	733348C	2	1	2	3	3	2	3	1	1	1	1	3	2	2	0	0	1	1	3	1	3	1
20	737508C	3	1	2	2	3	1	3	1	1	1	2	3	3	1	1	2	1	1	3	1	1	1
21	740476C	2	1	1	3	3	1	3	2	1	2	1	3	3	1	2	2	1	2	3	1	3	1
22	741347C	3	1	2	2	1	1	2	2	1	2	1	3	2	1	2	1	1	2	2	1	2	1
23	741815C	3	1	2	2	1	1	1	2	1	2	1	2	3	1	2	2	1	3	2	1	2	1
24	743647C	3	1	2	3	3	2	3	2	2	0	0	0	0	1	3	2	2	0	0	0	0	1
25	744413C	4	2	1	2	1	2	2	2	1	2	1	2	1	1	2	1	2	0	0	0	0	2
26	750269C	3	1	2	2	3	2	1	2	1	1	1	3	3	1	1	3	1	1	3	1	3	1
27	753459C	2	1	2	3	3	1	2	2	1	1	2	3	2	1	1	3	1	1	3	1	1	1
28	758624C	4	1	1	3	3	2	2	2	1	3	1	3	2	1	3	3	1	2	3	2	2	2
29	761679C	3	2	2	3	3	1	3	2	1	2	1	3	2	1	3	1	1	3	3	1	1	2
30	768089C	3	1	2	3	2	2	2	2	1	1	2	3	2	2	0	0	1	1	3	2	3	2
31	768959C	5	1	1	2	3	1	2	1	2	0	0	0	0	1	2	3	1	2	2	2	3	1
32	771362C	3	1	2	3	3	2	3	2	1	2	2	3	2	2	0	0	1	2	3	1	3	2
33	772344C	2	1	2	3	2	2	3	2	1	1	1	3	1	1	1	2	1	1	3	1	1	2
34	773086C	3	2	2	2	1	1	1	2	1	3	2	3	2	1	3	1	1	3	2	1	1	2
35	776051C	3	1	2	3	3	2	1	1	1	3	1	2	2	1	1	1	2	0	0	0	0	2
36	177945C	3	1	1	3	3	2	1	2	1	2	2	3	3	1	2	3	1	2	3	1	2	1
37	781960C	3	1	2	2	3	2	2	1	1	1	1	2	3	2	0	0	1	1	2	2	1	1
38	785621C	2	1	2	3	3	1	3	2	1	2	2	3	1	2	0	0	1	2	3	1	3	1
39	785748C	3	1	2	2	3	1	2	2	1	3	2	3	2	1	2	2	1	2	3	2	1	1

40	786560C	1	2	2	2	3	2	2	1	1	3	1	2	2	1	1	3	1	1	3	1	1	1
41	787172C	4	1	2	3	3	2	3	2	1	3	2	2	2	2	0	0	1	2	2	2	1	2
42	788938C	2	1	2	3	3	1	2	2	1	3	1	3	2	1	1	2	1	3	3	2	2	1
43	790962C	3	1	2	3	3	2	2	1	1	3	1	3	2	1	2	3	1	2	3	1	3	1
44	791569C	3	1	2	3	3	1	2	2	2	0	0	0	0	2	0	0	2	0	0	0	0	1
45	795825C	4	1	2	3	3	2	2	2	1	1	1	3	3	1	1	2	1	1	3	2	2	2
46	796830C	2	1	2	3	3	2	1	1	1	2	1	3	1	1	2	2	1	2	3	1	2	1
47	805444C	4	1	1	3	3	2	2	2	1	1	1	3	2	1	1	3	1	1	3	1	1	2
48	807561C	3	1	2	3	3	1	1	1	1	2	1	3	1	1	2	2	1	2	3	1	3	1
49	807675C	1	1	1	1	3	1	2	2	1	3	2	3	2	1	2	3	1	3	3	1	3	2
50	808584C	4	1	1	3	3	1	1	2	1	3	2	2	2	1	3	2	1	3	2	1	3	1
51	013907C	4	1	2	3	2	2	3	2	1	1	2	3	3	1	1	3	1	1	3	2	3	1
52	811788C	1	2	1	2	3	2	2	2	2	0	0	0	0	2	0	0	1	2	2	2	1	1
53	817418C	3	2	1	2	3	2	2	2	1	1	2	2	3	1	1	1	1	1	3	1	3	2
54	817847C	2	2	2	2	3	2	2	1	1	2	1	2	1	1	2	2	1	2	2	1	3	2
55	817986C	3	2	1	3	2	2	1	2	1	2	2	3	1	1	2	2	1	2	3	1	1	2
56	827546C	3	1	2	3	3	1	3	2	2	0	0	0	0	2	0	0	1	3	1	2	2	1
57	821282C	3	2	1	3	3	2	3	2	1	1	2	3	2	1	1	1	1	1	3	2	2	1
58	820317C	3	1	2	2	3	1	2	1	1	3	2	2	2	1	1	2	1	1	2	2	1	2
59	830102C	2	2	1	3	3	1	3	1	1	1	1	2	3	1	1	3	1	1	2	2	3	1
60	840289C	1	2	2	3	3	2	1	1	2	0	0	0	0	1	3	3	2	0	0	0	0	3
61	840482C	2	2	2	3	3	2	2	2	1	2	2	3	2	2	0	0	1	2	3	2	1	2
62	926929C	2	2	2	3	3	2	2	2	1	3	2	3	2	2	0	0	2	0	0	0	0	1
63	810734C	2	1	2	3	3	2	2	2	2	0	0	0	0	2	0	0	2	0	0	0	0	1
64	816178C	1	1	2	2	3	2	2	1	1	1	1	3	3	1	1	3	1	1	2	1	3	1
65	809999C	1	1	2	3	3	2	1	1	1	1	2	2	2	1	1	3	1	1	3	1	1	1
66	021731C	4	1	2	3	3	2	1	1	1	2	2	3	3	1	2	2	1	2	3	1	3	1
67	204461C	3	1	2	3	3	2	2	1	1	2	2	3	2	1	3	3	1	3	3	2	2	2
68	841721C	3	1	2	3	3	2	3	1	1	2	2	3	2	1	2	3	1	2	3	2	2	1
69	845549C	3	2	2	3	3	2	2	1	1	3	2	3	2	2	0	0	1	3	3	2	3	1
70	850636C	2	1	2	3	3	2	2	1	1	1	1	2	2	1	1	3	1	1	2	1	3	1

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